1970

Progress Report No. 6

Biomedical Computer Laboratory

PROGRESS REPORT

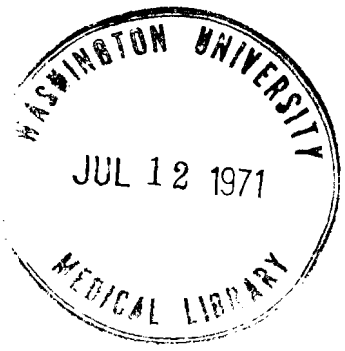
No. 6

1 JULY 1969 - 30 JUNE 1970

Biomedical Computer Laboratory
Washington University School of Medicine
St. Louis, Missouri

BIOMEDICAL COMPUTER LABORATORY

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE



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I. INTRODUCTION

This progress report from the Biomedical Computer Laboratory (BCL) summarizes work done during the period from July 1, 1969 through June 30, 1970. The Biomedical Computer Laboratory collaborates with research investigators throughout the Washington University School of Medicine in the application of advanced computer techniques to research problems in biology and medicine.

One class of applications requires strong coupling of the computer to its environment. These applications often involve the use of a Laboratory Instrument Computer (LINC) or a Programmed Console (PC). We have pursued these applications by bringing signals from the laboratories to BCL by means of either analog tape recordings or telephone lines and, more frequently, by taking the computers to the laboratory.

A second class of applications requires a computer strongly coupled to its environment and also the advanced information processing capabilities available on large central machines. To meet the demands of this particularly difficult class of applications we have connected most of our laboratory-style computers via telephone lines to the IBM 360/50 at the Washington University Information Processing Center.

A final class of applications requires extensive use of large-scale computational services. Many investigators are assisted in their research through the use of generalized numerical, non-numerical, and statistical routines. This work is carried out in part by staff members of BCL, but primarily by members of the Division of Biostatistics under the direction of Dr. Reimut Wette, and the University Computing Facilities Scientific Data Processing Group.

The Washington University Computer Laboratories (WUCL) is a federation of computer research activities including the Biomedical Computer Laboratory, the Computer Systems Laboratory, and the Computer Components Laboratory. This federation of laboratories functions through a coordinating committee composed of the three laboratory directors and in addition, R. A. Dammkoehler, C. E. Molnar, W. H. Danforth, and until his resignation in June, 1970, G. E. Pake.

The Computer Systems Laboratory, which is under the direction of Professor W. A. Clark, is active in the design, development and evaluation of a compatible set of "macromodules" from which arbitrarily large, complex, or specialized computer systems can be assembled.

The Computer Components Laboratory, under the direction of Professor W. N. Papian, is a part of the School of Engineering and Applied Science. The Laboratory performs applied research and development work in materials, devices, and circuits for advanced information processing systems.

A National Advisory Panel assists in planning health-related activities and presently has the following membership:

H. K. Beecher	Door Professor of Research in Anesthesia	Harvard Medical School
W. H. Danforth	Vice-Chancellor for Medical Affairs	Washington University School of Medicine
K. F. Killam	Professor of Pharmacology	University of California at Davis
F. M. Richards	Professor in Molecular Biophysics and Chemistry	Yale University
R. S. Snider	Professor of Anatomy and Director of Center for Brain Research	University of Rochester

The Advisory Panel meets periodically with the WUCL Coordinating Committee to review developing techniques and to advise upon desirable areas of application.

II. SOURCES OF SUPPORT

During the period covered by this report the primary source of support for the Biomedical Computer Laboratory was a grant from the National Institutes of Health:

RR 00396	A Resource for Biomedical Computing

Collaboration with other investigators often involved work already supported by other grants. Most of this support was from the National Institutes of Health:

AM 10025	Water and Electrolyte Transport in the Toad Bladder
CA 05139	Training on Radiation Therapy, Physics and Biology
CA 10435	Clinical Cancer Radiation Therapy Center Grant
CA 10926	Use of Heavy Isotopes in Biological Research
CA 04483	Effects of X-Ray on Normal and Malignant Cells
EY 00204	The Etiology of Reduced Visual Functions
GM 01747	Training Program in Radiology (Nuclear Medicine)
GM 14889	Cyclotron Produced Isotopes in Biology and Medicine
GM 17386	Scanner Computer Analysis of Radiographic Bone Images
HD 04014	Aldosterone Secretion During Growth and Development
HE 00082	Clinical and Experimental Research in Respiration
HE 10237	Physiological Relationship of Upper and Lower Airways
HE 10523	Pulmonary Circulator Dynamics During Lung Inflation
HE 11233	Sensitive Radioimmunoassay for Digitalis
HE 12839	Blood Degradation in Artificial Organs
HE 12237	Regional Cerebral Function: Radioisotope Methods
NS 03856	Auditory Communications and its Disorders
RM 00056	Cooperative Regional Radiation Therapy - Therapy Development Support Program

Atomic Energy Commission contracts helped to support portions of several projects:

AT(11-1)1653 Biologic Consideration in Anatomic Imaging with Radionuclides

AT(11-1)2011 A Method for the Determination of Regional Blood Flow in Tissues by Means of Stimulated X-Ray Fluorescence

AT(11-1)2089 Study of Elementary Particle Physics

Educational and General Funds from the Missouri Heart Association and a General Support Grant from the Hartford Foundation also helped to support portions of several projects.

III. PERSONNEL

EMPLOYEES

Personnel employed by the Biomedical Computer Laboratory during the period covered by this report were:

Director

Jerome R. Cox, Jr., Sc.D.

Assistant Director for Engineering

V. W. Gerth, Jr., M.S.

Administrative Officer

Edward L. MacCordy, M.B.A.*

Associate Professor

Donald L. Snyder, Ph.D., Electrical Engineering, since September 1, 1969*

Assistant Professors

William F. Holmes, Ph.D., Biochemistry
Maxine L. Rockoff, Ph.D., Applied Mathematics and Computer Science

Research Assistants

Robert J. Arnzen, Ph.D., since April 1, 1970*
Gerald R. Barthel, M.S.
James M. Baker, B.S.
Philip S. Berger, M.S., since March 11, 1970
G. James Blaine, M.S.
Andrew L. Bodicky, B.S.
Kenneth W. Clark, M.S., since January 21, 1970
Carol S. Coble, A.B., since August 7, 1969
James E. Crawford, III, B.S.
Ronald W. Hagen, M.S., since May 1, 1970*
Rexford L. Hill, III, M.S.
Sung-Cheng Huang, M.S., since September 1, 1969
Akihiro Ichijo, B.S., since September 1, 1969
Kenneth B. Larson, Ph.D., since March 1, 1970
Monte D. Lien, M.S.
Michael D. McDonald, B.S.
Joanne Markham, B.A.*
Nizar A. Mullani, B.S.
Floyd M. Nolle, M.S.
James M. Pexa, B.S.
Bruce F. Spenner, B.S., since September 1, 1969*
Elizabeth Van Patten, B.A.

Research Nurse

Dorothy M. McDarby, B.S., since February 16, 1970

Technical Assistant

Betty J. Greenwood, since October 23, 1969

Engineering Assistant

Glen M. Roa

Programming Assistants

Wilfred L. Anderson, B.A.
Adonis R. Black, B.S.
Douglas W. Clark
William V. Glenn, Jr., M.D.
Steven D. Iceland, B.A., since June 1, 1970
Richard A. Kolde, B.S.
John A. Parker, B.A., since October 3, 1969
E. D. Scheifler, since January 19, 1970
Geoffrey M. Waldron, since June 4, 1970
Louis J. West
Steven Ziskind

Project Technician

H. Dieter Ambos

Electronics Technicians

Charles R. Buerke
Christopher R. Fraction
Kenneth L. Kunkelmann

Machinist

George C. W. Meyer*

Librarian

Allie Allmon, B.S.*

Laboratory Assistant

Allen Sanders*

Business Manager

Virginia M. Bixon, B.S.

Secretaries

Merry M. Ambos
Christine Guerrero
Wanda J. Meek
Linda S. Russo, since January 22, 1970
Sandra Sfondouris, since May 25, 1970

*Indicates at least 50% of the individual's effort is supported by another laboratory or department.

Changes in Personnel

During the period covered by this report the following personnel resigned or completed their work at the laboratory:

Merry M. Ambos, terminated June 16, 1970
Gerald R. Barthel, terminated August 15, 1969
Adonis R. Black, terminated August 31, 1969
James E. Crawford, III, terminated December 12, 1969
Christine Guerrero, terminated November 28, 1969
Dorothy M. McDarby, terminated May 28, 1970
Donald J. Manson, terminated July 31, 1969
Glen M. Roa, terminated December 31, 1969

In addition, the following students worked at the laboratory for brief periods:

Douglas W. Clark, returned to school August 31, 1969
David Kaplan, returned to school August 31, 1969
Richard A. Kolde, returned to school August 31, 1969
Louis J. West, returned to school August 31, 1969, rehired June 8, 1970
Steven Ziskind, returned to school August 31, 1969

RESEARCH COLLABORATORS

During the period covered by this report the following investigators from other laboratories, departments, or institutions, collaborated with BCL staff members on problems of joint interest:

Washington University

R. Aaronson, Biochemistry
L. J. Banaszak, Ph.D., Physiology and Biophysics
D. Bates, B.A., Biochemistry

D. A. Bridger, Information Processing Center
L. Broch, B.S., Opthalmology
C. C. Carter, M.D., Neurology
R. E. Clark, M.D., Surgery
J. A. Collins, M.D., Surgery
E. Donnagan, Opthalmology
J. O. Eichling, Ph.D., Radiology
J. M. Enoch, Ph.D., Opthalmology
A. Feldman, Ph.D., Radiology
S. Garavelli, B.A., Biochemistry
J. C. Georgian, M.S., Mechanical Engineering
H. Fotenos, Radiology
C. Frieden, Ph.D., Biochemistry
T. L. Gallagher, Sc.D., Information Processing Center
R. Glenn, Radiology
D. Goldring, M.D., Pediatrics
S. Goldring, M.D., Neurosurgery
P. Handler, Ph.D., Computer Systems Laboratory
J. Hecht, A.B., Radiology
W. H. Holland, A.B., Psychiatry
B. L. Holman, M.D., Radiology
M. Lassen, M.Sc., Radiology
J. A. Lifton, B.S., Radiology
J. F. Lindeman, M.D., Radiology
V. Luthra, Mechanical Engineering
F. S. Mathews, Ph.D., Physiology and Biophysics
B. Milder, B.S., Opthalmology
G. C. Oliver, Jr., M.D., Medicine
G. T. Perkoff, M.D., Preventive Medicine
E. J. Potchen, M.D., Radiology
W. E. Powers, M.D., Radiology
S. D. Rockoff, M.D., Radiology
A. Roos, M.D., Anesthesiology and Physiology
J. H. Scandrett, Ph.D., Physics
S. Sutera, Ph.D., Mechanical Engineering
M. M. Ter-Pogossian, Ph.D., Radiology
L. J. Thomas, M.D., Anesthesiology
L. J. Tolmach, Ph.D., Radiology
M. J. Welch, Ph.D., Radiology
C. S. Weldon, M.D., Surgery
V. V. Weldon, M.D., Pediatrics
R. Wette, D.Sc., Biostatistics
G. A. Wolff, M.D., Medicine
A. R. Zacher, Ph.D., Physics

M. D. Anderson Hospital and Tumor Institute, Houston Texas

R. J. Shalek, Ph.D.
M. Stovall, B.S.

Central Institute for the Deaf

L. L. Elliot, Ph.D.
D. H. Eldredge, M.D.
I. J. Hirsh, Ph.D.
A. Nabelek, D.Sc.
I. Nabelek, C.Sc.
D. A. Ronken, Ph.D.
C. S. Watson, Ph.D.

Methodist Hospital, Houston, Texas

D. Brooks, M.D.
M. E. DeBakey, M.D.
C. J. Flynn, M.D.
D. H. Glaeser, Sc.D.
S. M. Rhode

National Cancer Institute, Bethesda, Maryland

F. Faw, B.S.
D. W. Glenn, M.S.
R. Johnson, M.D.

New England Medical Center, Boston, Massachusetts

P. W. Neurath, D.Sc.
D. A. Low, A.B.

Ontario Cancer Institute, Toronto, Canada

D. Brinkman, B.S.
J. R. Cunningham, Ph.D.
W. D. Rider, M.D.

Royal Marsden Hospital, Institute of Cancer Research, Surrey, England

R. E. Bentley, Ph.D.
J. Milan, M.S.

Stanford University, Stanford, California

C. J. Karzmark, M.D.
D. C. Rust

Temple University, Philadelphia, Pennsylvania

K. C. Tsien, M.A.
D. J. Wright, Ph.D.

University of Chicago, Chicago, Illinois

H. A. Fozzard, M.D.

University Hospital, London, England

J. S. Clifton, M.Sc., A. Inst. P.

Yale University, New Haven, Connecticut

A. L. Finn, M.D.

IV. PHYSICAL RESOURCES

On April 15, 1964, the Biomedical Computer Laboratory was formed and the original staff moved into 5,515 square feet (gross) of laboratory space at 700 South Euclid Avenue, just across the street from the main building of the Washington University School of Medicine. Equipment then available for laboratory applications of digital computers included a LINC (Laboratory INstrument Computer). This small stored-program computer has been designed specifically for use in biology and medical laboratories where there is a requirement for strong coupling between the computer, the investigator, and other experimental equipment. Since that time some twelve LINC's and five PDP-12's, a newer implementation of the LINC, have been added to the resources of the Washington University medical community.

In 1966 the Programmed Console was designed at BCL to function as a combined stored-program digital computer and remote display console for the IBM 360/50 installed during May, 1966, at the Washington University Information Processing Center. BCL's computational facilities now include three specialized Programmed Consoles built at the laboratory. In addition, thirteen Programmed Consoles have been built by SPEAR, Inc., from plans and specifications developed at BCL. Of these, six are now being evaluated under an NIH sponsored program as an aid to radiation treatment planning at radiology centers in Stanford, California; Bethesda, Maryland; Houston, Texas; Boston, Massachusetts; Philadelphia, Pennsylvania; St. Louis, Missouri; and Toronto, Canada. Two Programmed Consoles manufactured by SPEAR, Inc. are in use in other projects at BCL.

Other laboratory facilities include a data transmission distribution system, a well-stocked electronics shop, a large inventory of electronic and computer test equipment, a variety of digital system modules, and both analog and digital tape recorders.

During the past six years the laboratory space has been increased by 2762 square feet on the ground floor and 2742 square feet on the second floor of 700 South Euclid, and by 3463 square feet on the second floor and 1257 square feet of the basement of the building just south of the original space. Facilities for computational applications, laboratories, staff offices and a WUCL research library are provided in these acquired spaces. Direct communication with the IBM 360/50 at the Washington University Information Processing Center is provided via phone lines, Programmed Consoles and LINC's.

On October 1, 1969, an on-line computer monitoring system was installed by BCL in the Cardiac Care Unit of the Barnes Hospital complex. The computer equipment is housed in 360 square feet of specially designed space within the unit. Key BCL staff members occupy 260 square feet of office space nearby.

V. RESEARCH PROJECTS

The reports presented in the following sections are arranged according to the major research areas in which the laboratory has been active in applying computers to medicine and biology during the last year. Each report lists the personnel who participated in the research and gives their affiliation. The academic degrees of all BCL personnel are omitted in these lists since this information can be found in Section III. Unless otherwise specified, all organizations and departments listed are part of Washington University. Also listed, by grant or contract number, is the support for each research project. The titles of applicable grants or contracts and the funding agencies are provided in Section II.

Reference to other work described herein will be made by section number alone. References to any of the five previous BCL progress reports will be abbreviated thus: (see PR 3, B-6).

A. Radiation Treatment Planning

With the announcement by two manufacturers of plans to market radiation treatment planning systems based on work at BCL, this research area approaches a new phase. BCL will continue to support the original treatment planning programs, but major responsibility for new developments will be taken over by industry.

A-1. RAPID - Radioactive Point Implant Dosimetry

Personnel: E. Van Patten, BCL

Support: RR 00396

A program which calculates radiation intensities from needle implants and point sources has been in operation for several years on the IBM 360/50 (see PR 3, B-6). The PC has been used as the normal input-output to this program. The data is gathered using appropriate scope displays and stored on the disk at the 360 for later transmission to the batch partition for execution of the RAPID programs. The output is likewise stored on the disk in the form of 17 by 17 grids of points for each of five planes; these grids may then be brought into the PC where selected isodose curves are interpolated from them and displayed on the scope.

Two major drawbacks to this procedure have been the lack of a permanent copy of the output and the imprecision in the method of entering the location and orientation of the sources. To remedy the

first drawback, the option of plotting isodose curves for each of the five planes on the CalComp Plotter, has been added to the program. Identifying information is printed along with the curves. The latter drawback is being corrected by entering the locations of the sources with the aid of the rho-theta.

Besides these additions, the program's usefulness is being improved by making it easier to change existing data files, by allowing for the saving of either data or output and by improving recovery procedures after 360 or transmission failures.

A-2. Revision of Instruction Manuals for Radiation Treatment Planning

Personnel: B. J. Greenwoood, BCL

Support: RR 00396

To incorporate needed additions and revisions, clarify areas of confusion and provide a more easily read format, the following BCL monographs are being rewritten and consolidated:

54 Enter Patient Contour
65 Radiation Treatment Planning Programs
81 DMUTIL
96 CONSTANT
100 Datamaster Operating Instructions
105 Enter Doses

A standardized format was developed, and all the above documents are in the final stages of revision.

A-3. Annotation of Superimpose Beams

Personnel: B. J. Greenwood, BCL

Support: RR 00396

Complete annotation of the Superimpose Beams Manuscript was done to provide information necessary for modification of the program by PC users. In addition, the following information was compiled: flow charts for all subprograms, subroutines and overlays; a memory map; tabulations of tags and origins; "where used" charts of index registers and image registers; and a summary for each subprogram, subroutine and overlay listing all external and internal subroutines, index and image registers and data areas used.

A-4. PC Planner's Press

Personnel: B. J. Greenwood, BCL

Support: RR 00396

As an aid to PC users and other interested persons, a newsletter, the PC Planner's Press, is now published by BCL. It is designed to provide information concerning developments pertaining to the Programmed Console. Plans call for the newsletter to cover the following topics: review of publications and programs pertaining to the PC, descriptions of user's PC activities, clarification of problem areas concerning the operation of PC programs, and information on future PC users meetings.

A-5. PC Users Meeting

Personnel: V. W. Gerth, Jr., BCL
J. R. Cox, Jr., BCL

Support: RR 00396

A meeting of the users of PC's in Radiation Treatment Planning was held on August 15 and 16, 1969 in Boston, Massachusetts. The first afternoon was devoted to general discussion of the performance of the hardware and specific software questions. The major improvement in the system was traceable to the new Datamaster which provided increased reliability and inter-machine compatibility. Also, demonstrations of new graphic output devices were given.

The second day featured an informal report presented by each institution describing experiences with the PC in clinical use. BCL presented new developments underway and Spear, Inc. revealed plans for this new Radiation Treatment Planning System. A meeting for July, 1970 was planned at which drafts of final evaluation reports will be presented.

Institutions represented at the meeting include: M. D. Anderson Hospital, Houston, Texas; Institute of Radiation Physics, Stockholm, Sweden; Joint Center for Radiation Therapy, Boston, Massachusetts; Massachusetts General Hospital, Boston, Massachusetts; Memorial Hospital, New York, New York; National Cancer Institute, Bethesda, Maryland; National Institutes of Health (DRR), Bethesda, Maryland; New England Medical Center, Boston, Massachusetts; Ontario Cancer Institute, Toronto, Ontario; Royal Marsden Hospital, London, England; Temple University, Philadelphia, Pennsylvania; University Hospital, London, England; University Hospital, Lund, Sweden; Washington University, St. Louis, Missouri.

Interested equipment manufacturers present were Spear Computers, Inc., Bell and Howell, Inc., and Graphic Sciences, Inc.

A-6. TUB

Personnel: W. V. Glenn, Jr., BCL
A. L. Bodicky, BCL
A. Feldman, PhD., Radiology
R. Glenn, Radiology

Support: RR 00396
CA 10435
CA 05139
RM 00056

TUB is a PC program which drives a radiation detector through a field of ionizing radiation, measures doses at certain points, and produces a beam card for use in Superimpose Beams.

Major changes during the year in the TUB program as reported in PR 5, B-4 are few. Several methods of finding and following isodose lines through the water phantom in order to check interpolated isodose lines were tried before an accurate, fast algorithm was found. As an additional check, the probe can be driven down the beam's central axis in search of a selected isodose line; when found, the isodose line's position is then marked on the central axis. Finally, an "auto" option has been added. This option allows the operator to specify five isodose lines before scanning the grid for dosage measurements. As soon as the grid scan is completed the program automatically interpolates, follows, and marks on the central axis the previously specified isodose lines. Minor program changes were made to facilitate testing the number of samples necessary at each point, delay between each sample, and the accommodation of both moving and reference probes.

Current efforts center on checking linearity of the signal from probe to computer and finding the proper combination of damping, sampling speed, and delays. Attention is also being directed to checking experimental isodose charts against published standards.

When fully evaluated, the hardware and software created in this project will be used to generate beam libraries for standard and non-standard teletherapy beams at therapy centers in the Regional Medical Program. The present system is described in BCL Monograph 131 and 132.

Paper Presented:

W. Glenn, A. Bodicky, A. Feldman, and R. Glenn. "A Signal Plotter Operated Remotely Under the Control of a Small Computer," at the Fifty-fifth Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, Illinois, November 30-December 5, 1969

B. Electrocardiographic Rhythm Monitoring

The past year has seen a substantial increase in activity in the application of computers to the monitoring of arrythmias. A new Coronary Care Unit was opened, a monitoring system ARGUS (Arrythmia Guard System) was installed, and evaluation of its performance undertaken. To our collegues in the Division of Cardiology, Dr. Wolff and Dr. Oliver, must go a large share of the credit for the year's exciting developments.

B-1. Construction and Operation of the Barnes Coronary Care Unit

Personnel: G. Wolff, M.D., Medicine
F. M. Nolle, BCL
J. R. Cox, Jr., BCL
H. D. Ambos, BCL

Support: RR 00396
Barnes Hospital
Hartford Foundation
Washington University

On October 3, 1969, the Barnes Hospital Coronary Care Unit became operational, culminating one year of collaborative planning and seven months of construction (see (PR 5, C-1). During the construction phase, the above personnel acted in a daily, on-site advisory capacity. Although the details are too numerous to list completely, they included the following: exact location and configuration of services and fixtures, especially for the monitoring and communications systems; installation of equipment ground and signal ground both isolated from the metal conduit; installation of signal carrying conduits; cable pulling and terminations for signals leading from the bedsides, nurse stations, discussion stations, and computer room.

The digital computer system ARGUS for monitoring electrocardiographic rhythms (see PR 5, C-2) became operational in November, 1969, upon completion of cable connections for the system. Since then, the computer system has been in continuous operation, monitoring the ECG rhythm of any two patients selected by the CCU medical staff. During the first 9 months of operation, 600 patients have been admitted to the CCU and of these, 50% have had a diagnosis of definite or probable acute myocardial infarction.

B-2. ARGUS Processing Algorithms -- Implementation

Personnel: F. M. Nolle, BCL
J. R. Cox, Jr., BCL
J. E. Crawford, BCL
M. D. McDonald, BCL
G. C. Oliver, M.D., Medicine
G. Wolff, M.D., Medicine

Support: RR 00396
HE 11233
Hartford Foundation
Missouri Heart Association

ARGUS (Arrythmia Guard System) software development has proceeded along two pathways: the development of data compression algorithms for the Cycle Processor and the development of an extensive amount of additional software needed to provide an operational rhythm monitoring system with emphasis on detection of Premature Ventricular Contractions (PVC).

The Sample, AZTEC, and Primitive Processors operate as previously described (PR 5, C-3) except that, in addition to the QRS duration the Ventricular Primitive data now contains three additional descriptors of the QRS complex. These descriptors are labeled Height, Offset, and Area.

The QRS Height is a positive number corresponding to the vertical separation between the lowest and highest AZTEC bounds within or neighboring the QRS complex. The Offset is a signed number corresponding to the vertical distance from the baseline to the center of the QRS complex. The baseline is defined as the midpoint between the AZTEC bounds neighboring the QRS. The center of the QRS complex is defined as the midpoint between the lowest and highest AZTEC bounds within or neighboring the QRS. The Area is a positive number corresponding to the area of the waveform obtained by rectifying the QRS AZTEC with respect to the QRS baseline.

The Cycle Processor has undergone an extensive effort to develop an algorithm for grouping QRS complexes which are similar in shape. To achieve this, the shape of each QRS complex which occurs in artifact-free data is considered to be described by a point in four-dimensional space with coordinates of Duration, Height, Offset, and Area. The Cycle Processor assigns, to each such QRS, a catalog number between zero and fifteen identifying a history of measurements on QRS complexes which are judged to be similar in shape to the test QRS. This part of the Cycle Processor may be viewed as a placement agency which assigns each newborn QRS complex to one of sixteen possible families and merges the characteristics of the newborn with those of the family.

While a complete description of the placement procedure cannot be made here, the more important features can be outlined. Filed under each catalog number are the maximum and minimum values which have occurred for each of the four coordinates of members of the family. Also in the file are the total number of QRS complexes which have been assigned that number (the population of the family) and the total number of QRS complexes which have occurred since the last occurrence of a QRS with that catalog number (the age of the family). When a newborn QRS occurs, the Cycle Processor attempts to place it with an existing family in the same manner as voltage samples are grouped together into a horizontal line in the AZTEC Processor with the exception that the apertures for the four coordinates are proportional to the current maximum values. If one or more families is found acceptable, then the family with the youngest age is selected. If no families are found acceptable, then a new family is created. If room must be made for the new family, then the family with the oldest age is removed. Families may also be removed during the placement checking process if their age exceeds a maximum allowable age. One or more of the families may have an attached label indicating that their members are considered "Normal" QRS complexes for the patient. The maximum allowable age for families with a Normal label is much less than that for other families.

Upon initialization there are no families in the file so that the first QRS starts family number zero. The first family to be labeled Normal is one which has a population of five or more and which has the minimum duration of all families with populations of two or more. Once a Normal family is established, the Cycle Processor performs a cross-checking procedure for the family of each newborn QRS using the average coordinates of that family to determine if the family of the newborn should also be labeled Normal. Finally, if the youngest family of Normal QRS complexes becomes too old, then a reinitialization process sets all existing families to an equal status by removing all Normal labels, setting all ages to zero and all populations to one.

PVC Detection System - The first operational rhythm monitoring program provides for detection of PVC's, trend displays of PVC rate and heart rate per minute for intervals of up to twenty-four hours, and selected alarm displays with paper chart verification for bigeminy, runs of PVC's, and frequency of PVC's. The program utilizes PC core as follows: core resident programs include Sample, AZTEC, Primitive, and a portion of Cycle and occupy about 3100_8 locations. About 1400_8 additional locations are overlayed in sequential fashion from the Information Broadcast System. These successive layers of programs do the majority of the work of the Cycle Processor, PVC detection, alarm checking and verification, and displays. About 2100_8 locations are occupied by data produced

by the Sample, AZTEC, Primitive, and Cycle processors including the QRS cataloger. A total of 1000_8 locations are occupied by the trend data and an alarm history.

The current PVC detection algorithm depends strongly on the Cycle Processor placement procedure for QRS complexes and consists, in part, of an addition to that placement procedure. If the newborn QRS has been placed with a family which does not have the Normal label, then the minimum distance between the average coordinates of the family of the newborn and of all of the existing Normal families is used to determine if the shape is Abnormal or Questionable. These shape labels, used in conjunction with the QRS duration and a suitably determined measure of prematurity of the QQ interval allow detection of PVC's under a variety of rhythms in addition to Normal Sinus Rhythm, such as Atrial Fibrillation and Bundle Branch Block.

Displays - Several programs were written to provide displays to the viewer periodically or upon request. One of these displays allows the user to enable and disable each alarm and to view and set the alarm limits; another gives a history of which, if any, alarms have occurred and when. Six of them provide information on PVC rate and heart rate over the last 15 minutes in 1 minute intervals, the last three hours in 5 minute intervals, and the last 24 hours in 15 minute intervals.

The PVC and heart rate displays are each in two sections. One provides graphical information such as the data and the axes, using a line drawing subroutine; the other provides textual information such as axis labeling, patient name, bed number and date, using a character display subroutine. Each of these displays also provides the viewer with an indication of the accuracy of the data plot by displaying percentage data loss from 0 to 100 per cent using the same time axis as the data.

B-3. ARGUS Processing Algorithms--Preparation and Testing

Personnel: M. D. McDonald, BCL
J. E. Crawford, BCL
D. W. Clark, BCL
F. M. Nolle, BCL

Support: RR 00396

A number of programs have been written which help in the preparation and testing of the ARGUS Software. Most of these programs relate to the preparation of PC programs on the LINC8. One, AMBAGES, is used for testing the operation of PC programs.

IMPREP is a system of LINC programs written to enable the preparation of a tape image of the contents of a broadcast memory. Imbedded within a LAP6 - PC system by means of three special meta commands, it allows addition, rearrangement, and deletion of programs in the broadcast library. The three meta commands are FI, for filing a program on the image tape, FD for displaying the image directory, and FW for printing out the directory. Binary programs for either the LINC8 or the PC are broken up into segments of uniform size known as broadcast blocks, each of which is given an identification number and a load location. Each broadcast block is 100_8 words in length and the total image consists of 400_8 blocks (See BCL Monograph 119).

PCAP, the PC assembly program, has undergone several modifications to adapt it to the LINC8 - PC system (See BCL Monograph 41). The capability of using up to ten different symbol tables and switching between them at will has been added. The MS and symbol table listing routines were modified to run on the LINC8 with PROGOFOP. LAP6 was altered so the special, so called "free" meta commands need not begin with the letter F.

PROGOFOP, the PDP-8 program resident in the LINC8 for handling most of the LINC input-output commands, has been augmented. The most extensive addition was for the Motorola Printer which operates at 240 lines per minute (see PR 3, F-8). This addition allows selection of the output device (conventional Teletype or Motorola Printer) independent of other LINC8 software. The Motorola Printer is selected if its power is on, otherwise the Teletype is selected. PROGOFOP was also modified to interpret LINC8 OPR instructions for the CalComp Plotter, the Information Broadcast Receiver, and the LINC8-to-PC communications. These modifications occupy approximately 1400_8 locations in memory bank one and thus limit the user of the 4K LINC8 to operation in memory banks two and three, a situation similar to that in the classic LINC.

AMBAGES (which means roundabout or circuitous proceedings or ways) is a system of PC and LINC8 programs written to facilitate the testing and modification of programs running in the Broadcast system. Programs in the PC are run interpretively under the control of AMBAGES; input data is obtained from programs running in the LINC8. Debugging is done primarily at the LINC8 where requests for data or special stops can be initiated and displays and dumps received. An image area is maintained in the LINC8 which contains the information that would normally be in the location occupied by AMBAGES. In this 3-way connection between the PC, Broadcast and LINC8, the LINC8 is passive, never initiating any transfer to the PC until interrogated by the PC.

B-4. ARGUS Processing Algorithms--Evaluation

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Support: RR 00396
HE 11233
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A comprehensive, controlled experiment to evaluate the performance of an arrhythmia monitoring system will certainly involve a large expenditure of manpower and equipment. Thus, such an experiment can only be considered when special-purpose, preliminary tests are no longer able to uncover problem areas. Even special-purpose tests require substantial expenditures of time by persons performing the tests and also by those interested in understanding the results of such tests. It is the responsibility of the investigators to clearly define the conditions under which such tests were performed in order to facilitate understanding of the results and to avoid creation of false generalizations.

We have recently completed a two-month experiment to determine the performance of the current ARGUS algorithms for QRS shape classification and for detection of Premature Ventricular Contractions. In order to facilitate tabulation of results on a wide variety of QRS shapes, especially those of PVC's or suspected PVC's, we chose to study the performance on short segments of patients' electrocardiograms at the time that they received therapy for PVC's. In performing this experiment, the following protocol was followed:

1) Single lead ECG's of fourteen CCU patients plus an audio announcement of time of day were continuously recorded on analog tape.

2) Patient charts were reviewed daily for the administration of a lidocaine bolus and/or the initiation of an I.V. drip as therapy for PVC's.

3) Patients were rejected for inclusion in the study if,

a) the patient was previously included in the study, or

b) the patient was using an artificial pacemaker, or

c) the patient succumbed to secondary ventricular fibrillation.

4) For those patients not rejected for the above reasons, an attempt was made to select the starting point of the ECG record five to ten minutes prior to therapy. If this attempt was unsuccessful, then the nearest ECG record with some occurrence of possible PVC's was found.

5) The record prior to the starting point was played into the computer and the gain was adjusted so that the "normal" QRS height had approximately nominal value (this is the only adjustment allowed).

6) The record was rejected for inclusion in the study if the computer continuously detected artifact during this setup period (usually power line interference greater than the AZTEC aperture due to poor electrode application).

7) Computer analysis was then started at the selected starting point of the ECG record. AZTEC, PRIMITIVE and CYCLE data were collected on digital tape. The ECG waveform was continuously recorded on a paper chart recorder with time indexing marks to allow correlation with computer output. Data was collected for approximately fifteen minutes.

8) Each record was analyzed only once. The gain was not changed during the analysis.

9) At a later time, one of two cardiologists marked the ECG paper record, classifying each QRS complex. A beat-by-beat comparison was then made between the ECG strip marked by the cardiologist and a plot of the AZTEC-reconstructed ECG marked by the computer. The cardiologists were not shown the results until the end of the study.

During the two month experiment, records containing more than 49 thousand beats were obtained from 34 patients. Figure 1 depicts a gross summary of results. The computer correctly classified 3,129 (78%) of the 4,010 PVC's. As may be seen in the figure, the PVC's which were not classified as such by the computer are fairly evenly distributed in the remaining computer classifications. For example, 152 PVC's (3.8% of the total PVC's) were classified as abnormal shape but non-PVC because they were less than 6 percent premature. Thus, no single change in the algorithm will allow a marked improvement in the computer classification of PVC's. A detailed analysis of the results indicates that the QRS shape classification is working well, separating QRS complexes of different shape almost unfailingly. Thus, improvement in performance should be possible at the Sequence level which may make use of more context by the analysis of longer periods of data.

Figure 1

Cardiologist Marked

Computer Marked	N	AB	?	VE	PV	$\overline{QRS}$
N	38,595	17	7	0	50	0
?-$\overline{PV}$	3,646	60	49	5	298	18
A-$\overline{PV}$	83	30	114	14	152	3
(?-PV / A-PV)	38	20	82	0	3,129	122
Z	2,985	2	26	7	168	NA
$\overline{QRS}$	17	8	5	7	213	NA

Cardiologist Legend

N - Normal
AB - Aberrant Conduction
? - Questionable
VE - Ventricular Escape
PV - Premature Ventricular Contraction
$\overline{QRS}$ - Non-QRS

Computer Legend

N ___ - Normal Shape
?-$\underline{PV}$ - Questionable Shape, Non-PVC
A-PV - Abnormal Shape, Non-PVC
?-PV - Questionable Shape, PVC
A-PV - Abnormal Shape, PVC
$\underline{Z}$ - Artifact
$\overline{QRS}$ - Non-QRS

B-5. Signal Termination and Patch Panels for the Coronary Care Unit

Personnel: H. D. Ambos, BCL
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J. M. Pexa, BCL

Support: RR 00396

All analog and digital control signals are brought into the CCU computer room and terminated on terminal strips inside a 3 foot by 5 foot junction box. These terminal strips are arranged to make an easy distinction between patient beds, nurse stations, discussion stations, and patient computers, (PC's). All wires are harnessed and tied down to give a uniform appearance and make troubleshooting of input-output signals relatively simple.

From the main junction panel, cables are wired in parallel to an adjacent 3 foot by 5 foot junction box, containing the patch panel for the PC's and a patch panel for the tape recorders. The PC patch panel allows a patient to be selected for computer monitoring via one patch cable, which handles all input-output signals.

Signals brought to the computer room from each of the bedside monitors include: ECG, Pressure, Standby, Hi Alarm and Lo Alarm. Signals routed between the computer room and the nurse stations include: delayed ECG's for each patient and control lines which operate the nurse station chart recorders on computer generated patient alarms. Signals from the Discussion Stations are associated with the remote keyboards. A number of spare terminal strips and cables are available for future expansion, such as monitoring of the Special Procedures Room.

B-6. Solid State Keyboards for the Coronary Care Unit

Personnel: V. W. Gerth, Jr., BCL
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Support: RR 00396

For the three Discussion Stations, Honeywell Microswitch 64SW-1 keyboards were selected on the basis of reliability, quiet operation, and availability. This keyboard provides the full ASCII character set and features integrated Hall-effect switches requiring no mechanical contacts. For uniformity, the local PC keyboard and the control console switches were also changed.

A digital multiplexer was designed to allow any of the discussion station keyboards plus the local keyboard to be recognized automatically. Since the keyboards provide saturated logic levels, the multiplexer was constructed from DEC M-Series modules and the final code bus then translated to DEC, clamped negative logic levels for use within the PC. The code bus was expanded to seven lines to take advantage of the full capabilities of the 64SW-1.

Microswitch 1SN-1 switches were used for the control console and mounted in a linear array. The console functions were encoded using M-Series modules mounted in the vicinity of the multiplexer and logically superimposed on the keyboard bus. Reliability has been excellent with a demonstrated MTBF exceeding 6000 hours on the five keyboards currently in use.

B-7. Video Distribution System for the Coronary Care Unit

Personnel: G. J. Blaine, BCL
C. R. Buerke, BCL

Support: RR 00396

Various data displays are provided by each of the Patient Computers on storage oscilloscopes. The video distribution system makes these displays available to remote video monitors at the two nurse stations and the director's office. A scan converter at each oscilloscope provides a video signal which is routed via coaxial cable to a DYNAIR distribution amplifier with four isolated outputs. Coaxial relays which are controlled from rotary selector switches at each remote station provide signal selection of the desired output from the viewing station. A positive interlock is provided by digital logic to prevent "momentary" shorting of the outputs during the switching action.

B-8. Broadcast Information System for the Coronary Care Unit

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Support: RR 00396

The Broadcast Information System for the Coronary Care Unit consists of a central transmitter and local receivers for each of the PC's and, in addition, a receiver for the LINC8 Inquiry Station. The

LINC8 is also provided with an interface to permit loading and checking the core memory storage of the broadcast transmitter.

Assembly and preliminary stand-alone tests of the transmitter and receiver were completed previously (PR 5, C-4). The integration of the system into the Coronary Care Unit was carried out in two phases.

The first phase was a closed-loop test using the LINC8 and various data patterns. Test periods for each pattern lasted up to 2 or 3 days. The second phase of system integration was the test and debugging of the PC receivers. The real time clock (hours, minutes, seconds) was used to verify the operation of the PC receiver. Test programs for the PC were then loaded into the broadcast to allow performance evaluation of the entire system. The system has been in almost continuous operation since October, 1969 with a total of less than two days when the system was out of service.

B-9. Analog Tape Recorder Modifications for the Coronary Care Unit

Personnel: F. M. Nolle, BCL
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Support: RR 00396

The microphones of the two Ampex FR-100A tape recorders (see PR 5, C-2) were modified to automatically record the output of the Audichron SA time announcer. The Audichron's output was connected via the main computer room junction box to the microphone jacks. By pressing the enable switch the time announcement recording is bypassed and voice can be recorded in the conventional way. During playback of previously recorded data, an optional on-off switch is supplied to prevent the erasure of the old Audichron output by recording the current output. A special playback connector was added to each tape recorder enabling previously recorded data to be handled by the PC's.

B-10. Computer Hardware Development for the Coronary Care Unit

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Support: RR 00396

A number of modifications to the PC's and LINC8 in the Coronary Care Unit have been carried out to aid in the implementation of ARGUS.

PC Analog Buffer Amplifier. Amplifiers employing linear IC operational amplifiers were designed for buffering the ECG signals from the patient monitoring equipment. The characteristics provided were the following: differential input impedance of 40 kilohms, continuous gain adjustment from 1 to 15, voltage offset adjustment, output limited from 0 to -10 volts, and low pass filtering with 24 db/octave roll-off and a -3db point at 70 Hz in the ventricular channels and 20 Hz in the atrial channels.

PC Hardware Sample Instruction. The PC instruction SMX ν ($0 \leq \nu \leq 3$) has been modified so that execution of this instruction selects multiplexer channel ν and converts the analog voltage on that channel to an unsigned, twelve-bit number in the PC accummulator. Zero volts is converted to 0000 and -10 volts to 7776_8. The integer 7777_8 is not allowed in order to facilitate conversion of the sampled value to a ones-complement signed integer.

PC Broadcast Information Receiver. All PC central processor and I/O logic associated with the Datamaster and phone line communications was removed. A new IOT instruction was defined to request from one to seven consecutive blocks of 76_8 words each from the broadcast receiver, (see PR 5, C-4). The identifier is specified by the operand of the IOT instruction. Transfer of data from the broadcast receiver to memory operates in a manner similar to the Data Break of the PDP-8. After initiation of a transfer request, PC program operation is allowed to continue until the broadcast receiver finds a match with the requested identifier. At this time PC program operation is suspended upon completion of the current instruction and the requested number of blocks are read into memory starting with the next broadcast block. Upon completion of the transfer, PC program operation is resumed at the place where it had been suspended. Two new branch class instructions, BDN (BRN6) and BER (BRN7) may be used to test for completion of the transfer and for the occurrence of a parity error during transfer.

Other Digital I/O. Additional IOT instructions have been defined in the PC to allow communication with the LINC8, to sense status inputs and to provide control outputs. Dual, parallel pathways between the PC's and the LINC8 allow concurrent transfer of twelve-bit data or command words. A twelve-bit status input command allows the PC to determine the patient's bed number being monitored, the status of the bedside standby switch, and the discussion station selector switches, (all of which are control lines), and the status of the LINC8 to PC data pathways. Three bits of the control output register are currently in use, one to control the sample interrupt and two to drive relays for PC generated alarms.

Display. The PC display combination of a Tektronix 564 storage oscilloscope with an optically coupled video camera has been replaced by a Tektronix 4501 scan converter which provides in a single package a storage oscilloscope display and a video output.

Plotter. A CalComp 565 Digital Plotter was interfaced to the LINC8. Three PDP-8 IOT channels were installed to run each of the CalComp lines. These are Drum Up, Drum Down, Carriage Right, Carriage Left, Pen Up, and Pen Down.

Printer. A Motorola TP 4000 Teleprinter was interfaced to the LINC8. A PDP-8 IOT channel was added to work in conjunction with the PDP-8 interrupt to engage and disengage the printer clutch and print an arbitrary pattern of dots in a vertical column, seven high.

Digital Tape Units. Two additional tape units, unit 4 and unit 5, were added to the LINC8. These additional units are connected in parallel with units 0 and 1. The original LINC8 is prewired to handle up to eight tape units, therefore no additional logic wiring was required.

Data Communication. Dual, parallel pathways were added between the LINC8 and PC's allowing twelve-bit data words to be sent by the PC's and stored on LINC8 tape or temporarily in LINC8 memory. One PDP-8 IOT channel was added to the LINC8 enabling the LINC8 to initialize data transfer and select the appropriate PC. Simultaneous data transfers between the LINC8 and more than one PC is not possible, since the LINC8 can only communicate with one PC at a time.

PDP-8 Broadcast Information Receiver. Using two PDP-8 IOT channels, 1 to 7 consecutive blocks of broadcast information can be transferred to the LINC8 in a manner similar to that for the PC's. The PDP-8 Data Break is used for the transfer or broadcast information from the Broadcast Receiver to the LINC8 memory.

C. Regional Tracer Kinetics

This section contains reports on the application of computers to dynamic tracer studies both with a probe array and with a gamma ray camera. In general, we have concentrated on improved temporal resolution at the expense of spatial resolution. This work has been carried out in the laboratories of Dr. E. J. Potchen and Dr. M. M. Ter-Pogossian.

C-1. Applications of the Gamma Camera-PC System

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Support: RR 00396
AT 1653
HE 12237

A number of studies are underway using the combination of the gamma camera and PC described last year (PR 5, D-1). Several special purpose data collection programs, display programs, and IBM 360/50 FORTRAN programs have been written. These have been used with the system of programs also described last year (PR 5, D-1) in the following experiments.

Regional Cerebral Blood Flow. Regional cerebral blood flow (rCBF) has been studied using the regional cerebral blood flow programs developed previously. Studies in dogs have included the effects on rCBF of various perturbations including embolization and changes in pCO_2. Also, a number of studies were done on patients following angiography in order to assess the usefulness of the gamma camera for human regional cerebral blood flow measurements. The evaluation of the accuracy and significance of data collected from these studies is now underway.

Spirometer Controlled Measurements of Changes in Regional Lung Density. Changes in lung density as measured by the single deep breath method described previously (see PR 5, D-1) proved to be useful[1], but were difficult to obtain because patients were required to hold their breath for a long time to obtain reliable results. A wedge spirometer has been interfaced to the PC to allow collection of events from the gamma camera during selected portions of the respiration cycle of patients breathing normally.

A closed breathing system with the spirometer in the circuit is provided, and the volume signal is sampled by the PC every 0.1 second (see C-2). Four successive increasing or decreasing samples after a change in direction of the volume signal indicate a maximum or minimum has been passed in the respiration cycle. These current maxima (X_{MAX_i}) and minima (X_{MIN_j}) are used to calculate a running average maximum (Y_{MAX_i}) and minimum (Y_{MIN_j}) as follows:

$$Y_{MAX_i} = \frac{X_{MAX_i} + Y_{MAX_{i-1}}}{2} \qquad i=2, \ldots .$$

$$Y_{MIN_j} = \frac{X_{MIN_j} + Y_{MIN_{j-1}}}{2} \qquad j=2, \ldots .$$

$$Y_{MAX_1} = X_{MAX_1} \quad , \quad Y_{MIN_1} = X_{MIN_1}$$

This has the effect of low-pass filtering the peak values to provide smoothly changing values of Y_{MAX_i} and Y_{MIN_j}.

Thresholds are calculated from the current averaged maximum (Y_{MAX_i}) and the current averaged minimum (Y_{MIN_j}) as follows:

$$\text{Upper Threshold} = Y_{MAX_i} - \frac{1}{8}\left(Y_{MAX_i} - Y_{MIN_j}\right)$$

$$\text{Lower Threshold} = Y_{MIN_j} + \frac{1}{8}\left(Y_{MAX_i} - Y_{MIN_j}\right)$$

New thresholds are calculated each time a new maximum or minimum has been detected. Using the thresholds to control input from the gamma camera, data are then collected in two 32 by 32 arrays, one each for inspiration and expiration. The resulting expiration array is subtracted from the inspiration array and the 32 by 32 differences are presented as percentages of the average difference. The results, which represent changes in density between inspiration and expiration, are displayed as contour plots.

Measurement of Regional Lung Ventilation. This procedure uses the washout of inhaled xenon 133 to calculate an index of ventilation. The patient sits with his back to the gamma camera and breathes from a bag containing xenon 133 mixed with air. Collection of a 16 by 16 data array begins when the isotope has reached equilibrium in the lungs; the collection time is also recorded. After several seconds, the xenon-air source is removed and the patient begins to breathe fresh air. Simultaneously the program begins collection of a second data array. The first frame of data is divided by the collection time to yield an array of equilibrium count rates. This rate for each cell is then divided by the total number of counts in the cell during washout (i.e., the second data array). The resulting indices of ventilation are normalized and contours of equal index are plotted.

Measurement of Changes in Lung Blood Flow. A special program written for this procedure collects data from the gamma camera in two 32 by 32 arrays; the collection time is variable with the entire procedure usually lasting about 15 minutes. The patient lies down with his back to the camera, an injection of indium 113 colloid is given, and the data are collected until a predetermined number of counts have been recorded. The data collection is then halted, and a drug such as phentolamine is injected. After a few minutes during which the drug takes effect, a second injection of indium 113 is given, and data are collected as for the first injection. The resulting data are presented in three contour plots. The data for each injection are normalized to the maximum count rate to give contours of equal count rate as a percent of the maximum rate. Then the original data are corrected for decay, and the signed percent change in count rate from the first injection to the second is calculated. Contours of equal percent change are plotted.

(1) Potchen, E. J., Evens, R. G., Hill, R. L., Adatepe, M., Holman, L., Lindeman, J. and Markham, J., "Regional Pulmonary Function in Man; Quantitative Transmission Radiography as an Adjunct to Lung Scintiscanning," The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 108: 724, 1970.

C-2. Spirometer Interface to PC

Personnel: R. L. Hill, BCL
C. Buerke, BCL

Support: RR 00396

A wedge spirometer has been interfaced to the PC to allow computer monitoring of respiration during gamma camera studies of the lung. Two electrical signals are available from the spirometer, one proportional to volume (0-10 liters), and the other proportional to flow (±1 liter/second). These signals are fed through operational amplifiers to match their full-scale range to that of the analog inputs of the PC.

C-3. Data Collection and Processing for Radioisotope Probes

Personnel: J. M. Baker, BCL
R. L. Hill, BCL

Support: RR 00396

A package of three programs for the PC has been written to implement the collection and analysis of regional blood flow data acquired by a set of six radioisotope probes. The first program of the package enables the user to compose a Datamaster timecard that specifies the number and duration of collection intervals for the probes. The second program is the data collection program for the probes which uses the timecard written by the first program. The data may be recorded on Datamaster cards or stored on magnetic disc at the IBM 360/50 via telephone lines. The third program uses the data collected by the second program to calculate blood flow in the region of any probe according to the method of Zierler[1].

(1) Zierler, K. L., "Equations for Measuring Blood Flow by External Monitoring of Radioisotopes," Circulation Research, 16: 309, 1965.

C-4. Display of Static Gamma Camera Images

Personnel: J. M. Baker, BCL

Support: RR 00396

Several programs have been written for the PC and the LINC to explore various means of displaying static radioisotope distributions as detected by a gamma camera (see PR 5, D-2).

A subroutine has been written for the PC to display contour lines of equal intensity for a 16 by 16 array. Further use has been made of such "isointensity" contours for a 32 by 32 array with the addition of a program that displays bands of similar intensity. The band width is determined by a specifiable multiple of the square root of the intensity value at the center of the band.

PC programs have also been written that present the 32 by 32 array in terms of alphabetic or numeric characters. In these displays, the relative intensity in each of the elements in the array is reflected by the numerical value or by the position in the alphabet of the displayed symbol.

Isometric displays of a 32 by 32 array have been adapted for the LINC. These displays present a two-dimensional histogram in three-dimensional perspective.

Programs have been written for the PC that yield gray scale pictures by varying the exposure of photographic film. One program displays one of several patterns whose brightness is proportional to the intensity of the array element. Another program displays a single pattern a variable number of times to create shades of gray. Methods of contrast enhancement including background cut off, high intensity cut off, spatial averaging and smoothing, and variable contrast, have been applied to these pictures.

C-5. A Utility Program for Dynamic Gamma Camera Data

Personnel: R. L. Hill, BCL
J. M. Baker, BCL

Support: RR 00396

A utility program for the PC has been written to be used in the programming system for the gamma camera (see PR 5, D-1). This utility program may be used to write collected data onto Datamaster cards, to print collected data on the Teletype, or to read previously recorded data from Datamaster cards for output.

C-6. Gamma Camera Interface to the PDP-12

Personnel: R. L. Hill, BCL
J. R. Cox, Jr., BCL

Support: RR 00396
AT 1653
HE 12237

An interface for the Digital Equipment PDP-12 has been designed for processing events from the gamma camera. The interface is similar in many respects to that designed for the PC (see PR 5, D-1).

The EG&G analog-to-digital converters used in the previous system will be used temporarily until selection of a faster converter is made. The outputs of the converters are used to address a memory location as before, but incrementing of that location is accomplished through the Data Break feature of the PDP-12 in 2.8-4.4 microseconds.

The control panel and patch panel of the previous system are replaced by an IOT instruction which enables and disables the interface, selects array size, directs arrays to specific areas of memory, and chooses options or fixed or variable dead-time, inscribed or circumscribed square, and fixed or variable duration of time per data frame.

The real-time clock of the PDP-12 is used to time the collection of data frames and out-of-range events are counted externally so as to require no computer time to process these events.

Publication:

Cox, Jr., J. R. and Hill, R. L., "Design Considerations for Interfacing Computers to Gamma Ray Cameras," presented at the First Biennial Conference on Quantitative Organ Visualization in Nuclear Medicine, Miami, Florida, May 5-9, 1970, (BCL Monograph 130).

C-7. Retrieval of Gamma Camera Data via 35mm Photographic Film

Personnel: J. H. Scandrett, Ph.D., Physics
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J. M. Baker, BCL

Support: RR 00396
GM 17386
AT 2089

A system has been developed to collect gamma camera data of dynamic radioisotope distributions via 35mm photographic film and to retrieve the data by detecting the regional transparency of the film with a flying spot densitometer under program control of the University's IBM 360/50. A motor driven 35mm camera is used to record successive frames of scintillation images as they are represented on a cathode ray tube of a gamma camera. The data are retrieved from the film by counting the apparent number of scintillation images on multiple regions of each frame of film; the counting is accomplished by very closely spaced density measurements of the film with the flying spot densitometer.

C-8. Tracer Kinetics Using Short-Lived Isotopes

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Support: RR 00396
GM 14889

Three major radioactive isotopes, oxygen 15, carbon 11, and nitrogen 13, are produced by the cyclotron at the Washington University School of Medicine for use as tracers in research and clinical studies. These short-

lived isotopes with decay half-lives of 124 seconds, 20 minutes, and 10 minutes, respectively, may appear to preclude their usage in most clinical studies. However, in dynamic studies the short half-life is a desirable attribute because usually it can be administered in large quantities affording good counting statistics with a relatively low radiation dose absorbed by the patient.

A method for the *in vivo* determination of regional cerebral blood flow (rCBF) and regional cerebral oxygen metabolism ($rCMO_2$) employing radioactive oxygen 15 has been developed[1]. In this approach, a small volume (<2 ml) of the patient's blood labeled with oxygen 15, either in the form of ^{15}O-water or ^{15}O-oxyhemoglobin, is pulse-injected selectively into an internal carotid of the patient. Regional cerebral blood flow is calculated from constants obtained from the analysis of the ^{15}O-water clearance curve. A constrained three-compartment steady-state closed mammillary system has been proposed to justify the method of analysis since recycling of the tracer markedly complicated some of the mathematical considerations. The close correlation between regional cerebral blood flow determinations obtained simultaneously with ^{15}O-water and ^{133}Xe dissolved in saline support the method of calculation employed.

Regional cerebral oxygen metabolism is obtained from knowledge of the fraction of the injected ^{15}O-oxyhemoglobin that is converted to labeled water during the passage of the injected bolus through the cerebral hemisphere. This parameter combined with the arterial blood oxygen content and the regional cerebral blood flow determined with ^{15}O-water permits the calculation of the regional oxygen metabolism or utilization. Values thus obtained in "normal" subjects agree favorably with published values of whole brain oxygen consumption.

Carbon 11 is used to label two substances, carbon monoxide, and glucose. The carbon monoxide is used to label carboxyhemoglobin for the purpose of *in vivo* visualization of blood pools such as spleen and heart, and also to investigate the usefulness of ^{11}C-carboxyhemoglobin as a tracer for the determination of total body blood volume. Investigations are under way for utilization of ^{11}C-glucose in two areas: (1) as a brain-scanning agent used specifically to visualize neoplasms in subjects for which there is no breakdown of the blood-brain barrier precluding visualization with currently used radiopharmaceuticals; and (2) assessment of the rate of glucose metabolism in the brain in the hope of finding some correlation between pathology and the utilization of this primary metabolite in the brain.

Nitrogen 13 has been tagged to the ammonia ion NH_4^+ and its possible uses as a clinical radionuclide are being investigated.

The gamma ray radiation from these isotopes is detected by six NaI (thallium activated) scintillation detectors that have been interfaced to the LINC computer (see C-9). A complete software package has been developed to aid in data acquisition, analysis, storage, plotting and display (BCL Monograph 126).

Data Acquisition and Storage. The contents of the six-bit counters in the interface (see C-9) are transferred to the LINC memory every millisecond and the number of events registered by the different probes summed in double precision for an interval of time specified by the program. A total of 126 such time frames can be collected for each probe ranging from 0.1 second to 100 seconds per time frame. Eight different time schedules comprising different combinations of such time frames are available to the researcher. The data collected are stored on LINC tape at the end of the run in a format whose index structure is compatible with that of LAP6.

Decay Correction. Since most of the radionuclides used have decay half-lives comparable to the duration of the experiment, it is essential that each data point be corrected for decay. The physical decay of the isotope given by the form $A = A_0e^{-\lambda t}$ may be corrected by multiplying each point by $e^{+\lambda t}$, where A_0 is the original value, A the observed value after a time t, and λ the decay constant. Values of λ tabulated are those for ^{15}O, ^{11}C, ^{13}N, ^{123}Xe, ^{133}Xe. Immediate plans include corrections for background and deadtime losses for each probe.

Plots. A variety of linear and semilog plots of the data are available on the Houston Omnigraphic Digital Plotter. In the linear plots a choice of three time scales is offered for a plot of counts per second versus time: 15 seconds, 30 seconds, and 900 seconds. The plots are automatically scaled to a maximum of 750 cps, 1500 cps, 3000 cps, 6000 cps, 12,000 cps or 24,000 cps.

Two different versions of the semilog plots are available on Houston 3 cycle semilog chart paper; 10 cps - 10 kcps and 100 cps - 100 kcps. The 10 cps - 10 kcps plot is offered for a fixed time scale of 1400 seconds maximum while the 100 cps - 100 kcps plot has a choice of 35 seconds, 70 seconds, 700 seconds, 1400 seconds, and 4200 seconds. Each plot also offers the option of a line plot or a point plot.

Display and Digital Printout. A quick look at the data is offered by a display program which shows any 400 second segment of the clearance curve. The time segment being observed may be shifted in time by knob 0 on the LINC console. Digital printout of the patient information, time schedule used, and the data for the six probes are also available on the Teletype.

Data Analysis. Two approaches were taken to aid in the data analysis of the washout curves. One approach was to utilize the SAAM program on the IBM 360/50 (see C-10) and the other was to emulate on the LINC a manual curve peeling technique that has been routinely used in the past. A prototype of this program has been written and results are encouraging. A more general version of this program is under consideration.

(1) Ter-Pogossian, M. M., Eichling, J. O., Davis, D. O., Welch, M. J., and Metzger, J. M., "The Determination of Regional Cerebral Blood Flow by Means of Water Labeling with Radioactive Oxygen-15," Radiology, 93: 31, 1969.

C-9. Six Probe Interface to the LINC

Personnel: N. Mullani, BCL
R. L. Hill, BCL

Support: RR 00396

An interface to the LINC has been designed to allow accumulation of histograms of count-rate vs. time as measured by six individual scintillation detectors, used for the study of cerebral blood flow using short-lived isotopes (see C-8).

Six six-bit scalers are provided in the interface and can be transferred directly into memory using an OPR instruction in the GULP mode of data transfer. A subroutine has been written that can interrogate these scalers and add their contents into 24-bit words in one millisecond, giving a probability of overflow for the scalers of less than 10^{-10} for count rates of up to 25,000 counts per second for each of the six probes.

C-10. Exponential Fitting of Radionuclide Data

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Support: RR 00396
AT 2011
GM 14889

Studies using the IBM 360/50 have begun to determine the best numerical technique to use in a LINC program for automatic exponential fitting of radionuclide data (see C-8). Initially the results of

graphical analysis were compared with results from SAAM (see F-13). The data were fit to a function of the form

$$Ae^{-k_1 t} + Be^{-k_2 t} + C$$

in 12 cases. The disagreement between the values was less than 20% in 7 of the 12 cases but was as high as 65% in 1 case. The deviation appeared somewhat systematic in that SAAM produced smaller values for A than did graphical analysis in 10 of the 12 cases. It is felt that this discrepancy is attributable to the fact that in the graphical analysis procedure there is a correction for data losses due to deadtime. The deadtime correction is anticipated to be of the form $m = \frac{n}{1-\tau n}$ where m is the true count rate, n is the observed count rate and τ is the deadtime of the detector and associated electronics. This is currently being studied to verify the deadtime correction. The resulting correction will be incorporated in the automated procedure.

Investigations are also underway to determine an automatic correction for background radioactivity. Since the radionuclide (oxygen 15) used in these experiments is short lived, the background radiation can become a significant part of the total measured radioactivity toward the end of the experiment. The effect of this is seen in some studies where the values of the last few data points, after being corrected for decay, increase.

Finally, some studies on the IBM 360/50 of different numerical methods for the calculation of the best least-squares parameters have been started. The magnitude of the decay rates k_1 and k_2 is about 10^{-6} times the magnitude of the coefficients A, B and C. This leads to the inversion of ill-conditioned matrices in the straightforward application of Newton's method for solving systems of nonlinear equations. This difficulty could be avoided (as it is in SAAM) by iteratively making a two parameter correction for the decay rates (solving a 2 by 2 system of linear equations) and then calculating the corresponding coefficients by solving a 3 by 3 system of linear equations.

C-11. In Vivo Flow Studies by Means of Excited X-Ray Characteristic Radiation

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J. O. Eichling, Ph.D., Radiology
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Support: RR 00396
GM 14889
AT 2011

Regional blood flow can be determined *in vivo* in various organs by injecting an identifiable indicator into the artery feeding the organs and by measuring, as a function of time, the passage of this indicator through the observed volume of tissue. The presence of a high atomic number indicator (typically iodine) is detected and measured by stimulating its characteristic x-ray fluorescence with a narrowly collimated beam of x-rays and by detecting this characteristic radiation by means of a lithium-drifted silicon x-ray spectrometer. The volume under observation is the common volume formed by the beam of x-rays and by the cone of acceptance of the collimator for the x-ray spectrometer.

In order to compensate for x-ray intensity fluctuations and for absorption variations, two-channel pulse height discrimination is used. The energy settings for the two windows are such that one of them will accept the major component of the characteristic radiation (C_1) and the other is displaced by approximately one kiloelectron volt from the characteristic radiation accepting only scattered radiation (C_2). The signals C_1 and C_2 are collected via the LINC and stored on tape. Following the experiment, the calculation

$$\frac{C_1 - C_2}{C_2}$$

is made for each data point. This value represents the intensity of a component of the charcteristic radiation normalized to the value of the scattered radiation reaching the detector, but with an energy very close to that of the characteristic radiation. The graphs of

$$C_1 \ , \ C_2 \ , \text{ and } \frac{C_1 - C_2}{C_2}$$

versus time can then be plotted by the LINC and Houston Omnigraphic Plotter.

In preliminary studies, this method has shown very good three-dimensional localization with a sensitivity of approximately 0.05% of iodine per gram of tissue. The counting rate obtained with a 70 kilovolt source of x-rays operated at 3 milliamperes at a distance of 2 feet from the target volume and with a characteristic radiation detected with a 25-square millimeter lithium-drifted silicon crystal placed at approximately 1 foot from the target volume and with the target volume of 1 cubic centimeter containing 1% iodine, was found to be approximately 100 counts per second. This counting rate is insufficient for dynamic studies for which a minimum of several thousand counts per second is desirable. However, this result can be achieved by increasing the x-ray tube current to approximately 50 milliamperes and by increasing the size of the detector to about 300 square millimeters. These changes are now under investigation.

C-12. Radio-Gas-Liquid Chromatograph System for the Classic LINC

Personnel: N. A. Mullani, BCL
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Support: RR 00396
GM 14889

The technique of Radio-Gas-Liquid Partition Chromatography is used in the division of Radiation Physics at Washington University for the purposes of: (a) studying the radiochemistry of cyclotron targets with potential for forming radionuclides of medical interest and (b) checking the purity of radiopharmaceuticals currently being used in animal or patient studies.

An interface has been designed to link a chromatograph to the LINC computer. The "mass" signal from the hot wire detector is first amplified and then digitized by a twelve-bit analog-to-digital converter. The radioactive data from a proportional counter are summed in a buffer register for a period of time controlled by the collection program. The digitized data are then transferred to the LINC accumulator by the execution of certain OPR instructions in the collection subroutine.

The complete software package for this system is under development and will consist of data acquisition, decay correction and analysis, plotting, display, digital printout and filing programs.

C-13. Parameter Estimation for Radioisotope Tracer Data

Personnel: D. L. Snyder, BCL

Support: RR 00396

A study has been undertaken to develop efficient computer oriented techniques for processing radioisotope tracer data obtained from gamma cameras and probe array detectors. The detector data has been modeled mathematically as a collection of inhomogeneous Poisson processes with associated intensity functions that are modulated by parameters characterizing the organ or tissue being monitored. The commonly used procedure for estimating the parameters is to least-squares curve fit assumed forms for the intensity functions to count-rate histograms. However, when the count rate is not sufficiently high, histograms are noisy and curve fitting procedures do not work well. To overcome this, we have been working toward using the additional information about the parameters contained in the event times of the observed processes. This implies more data gathering than that needed to form count histograms, but initial simulation studies indicate that parameters can be estimated accurately even when the count rate is quite low.

The approach we have taken is to describe the time evolution of the posterior statistics of the parameters of the intensity function as the count data are collected. The description is in the form of a differential equation that is compatible with computer implementation. Thus far, we have evaluated the approach by simulations and the results are encouraging. We plan in the near future to try the approach on real data obtained by monitoring oxygen 15 decay. The three monographs cited below describe the details of the approach and contain our initial simulation results.

Snyder, D. L., "Estimation of Stochastic Intensity Functions of Conditional Poisson Processes," submitted to the IEEE Transactions on Information Theory for publication. (BCL Monograph 128)

Snyder, D. L., "Detection of Nonhomogeneous Poisson Processes Having Stochastic Intensity Functions," submitted to the IEEE Transactions on Information Theory for publication. (BCL Monograph 129)

Snyder, D. L., "Filtering for Independent Poisson Processes Having Stochastic Intensity Functions," and "Parameter Estimation for Radioactive Tracer Data," to be presented at the UMR-Mervin J. Kelly Communications Conference, Rolla, Missouri, October 1970. (BCL Monograph 136)

C-14. Mathematical Modeling of Arrival and Washout of Diffusible and Nondiffusible Tracers in Measurements of Regional Cerebral Blood Flow

Personnel: K. B. Larson, BCL
J. R. Cox, Jr., BCL

Support: RR 00396

In the method of measuring regional cerebral blood flow (rCBF) described by Ter-Pogossian, et al.(1), radioactively-labeled water is injected into the internal carotid artery of a subject (see also C-8). Subsequently, the rate of washout of tracer from various regions of the brain is measured by monitoring the radioactivity through use of external detectors. Additionally, the mean transit time for blood flow through a region is determined by substituting radioactively-labeled carbon monoxide for the water as the tracer in the procedure. The labeled carbon monoxide is bound to the hemoglobin and hence cannot diffuse into the brain tissues. On the other hand, the labeled water diffuses through the tissues at a rate which is determined essentially by the self-diffusion coefficient of water. Measurements of rCBF are not affected by tissue diffusion after relatively long washout times when diffusion is no longer rate-limited; however, during the initial portion of the experiment, diffusion may play an important role in determining the shape of the response curves.

A mathematical model describing the arrival, uptake in tissue, and washout of tracer in measurements of rCBF has been developed in order to study the extent to which passive diffusion processes govern the response curves obtained. In this model, the assumption is made that the arrival rate of tracer in a region is a function only of anatomical factors and is independent of the chemical identity of the tracer. The arrival rate is determined from the carbon monoxide response curve by making use of the fact that the tracer is entirely confined to the vascular bed and by invoking the additional assumption that the washout rate is proportional to blood flow rate. A diffusible tracer arriving at this same rate is partitioned between blood and tissue, with tissue uptake rate controlled by diffusion. Washout rate is again taken proportional to blood flow rate, and now release of tracer from tissue is assumed to be diffusion-controlled. Moreover, it is assumed that the concentration gradients in the blood are very small relative to those in tissue, and therefore that the blood concentration is spatially uniform in the region being monitored. Equilibrium in the partition of substance between blood and tissue is assumed to exist only at the blood-tissue interface which is identified with the capillary walls.

A solution to the boundary-value problem posed by the model has been obtained. Using the resulting functions, a digital computer program

has been written to study the effect of varying the anatomical and physiological parameters, as well as the diffusivity of tracer substance. The possibility of using the model in data reduction for estimating values of specific regional flow rates will be examined.

(1) Ter-Pogossian, M. M., Eichling, J. O., Davis, D. O., Welch, M. J., and Metzger, J. M., "The Determination of Regional Cerebral Blood Flow by Means of Water Labeled with Radioactive Oxygen-15," Radiology, 93: 31, 1969.

C-15. Mathematical Studies of Large-Scale Diffusion of Labeled Substances in Poorly-Perfused Regions of Brain Tissue

Personnel: K. B. Larson, BCL
J. R. Cox, Jr., BCL

Support: RR 00396

A clinical application of measurements of regional cerebral blood flow consists of the detection of a poorly-perfused region of brain tissue indicative of the possible existence of a pathological state. With a given attainable spatial resolution, the question naturally arises as to the minimum volume of poorly-perfused tissue which can be detected. Mathematical modeling of this problem has been initiated, but has not yet been brought to a useful stage.

C-16. Randomly Branching Model for Simulating Transit Time Curves

Personnel: S. C. Huang, BCL
J. R. Cox, Jr., BCL

Support: RR 00396

The pattern of flow of an elemental volume of blood in the circulatory system can be described by a randomly branching process. At a vessel bifurcation a branching event occurs in the model process and the chance of such a branching event is determined by a probability density function of the random variable, branch length.

According to this model, the following quantities can be simulated or estimated:

Transit time curves. Transit time is the time required for blood to go from a point upstream to some point downstream. Due to the variety of velocities and paths associated with the elemental volumes of blood, two such volumes starting at the same time and place may not reach the

same destination simultaneously. Transit time therefore does not have a single value, but rather a distribution of values. This distribution can be calculated from the basic distributions of branch lengths and areas.

Regional blood volume. From the distributions of branch lengths and areas, the probability distribution of the total volume can be found. Using regional tracer data and either minimum-mean-square or maximum-likelihood estimation, it may be possible to estimate the blood volume of a region. Some preliminary results in the form of simulated curves have been obtained and are encouraging.

D. Monitoring the Critically Ill

A new research area building on previous work in cardiology has begun to develop during the past year. A strong stimulus to this work has been the growth of an active Cardiothoracic Surgery Division under the leadership of Dr. C. S. Weldon. The experience gained in the Coronary Care Unit and the Catheterization Laboratory will be invaluable in the further development of this research area.

D-1. Design of a Cardiothoracic Operating Room System

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C. S. Weldon, M.D., Surgery

Support: RR 00396
Washington University
Barnes Hospital

The physical design of a contemporary surgical operative system was organized into four basic parts: (1) material, equipment and personnel logistics, (2) microorganism control, (3) environmental control and (4) patient monitoring.

Logistics determined the floor plan with the operating room (OR) as a hub, surrounded by the supporting activities: sterile supply room, locker-scrub room, and anesthesia preparation room.

Microorganism control necessitated the installation of smooth, hard and abrasion-resistant surfaces. Chemical cleaning, auto and gas clave facilities provide biomass and colony control. Staged pressurization of compartments prevents intrusion of pathological microorganisms from lower to higher ordered sterilized compartments. Superfiltered air in the OR was specified to remove dust as small as .1 micron at 99% efficiency and to reduce transmission of aerobatic microorganisms. The OR air system provides a purging laminar (planar) flow at 21 feet per second over the patient and surgical staff, reducing reentry of microorganisms into surgical space.

Environmental control of the OR provides for filtered, cooled or heated, humidified air with the options of zero to one hundred percent fresh air. Lighting is fluorescent in a ring over the patient and surgical team. Optional spot operative lighting gives one to eight modulated beams.

Facilities for patient monitoring are provided for by a pedestal mounted on the OR floor at the head of the operation table, and containing oxygen, vacuum, 120V AC power, nine conduits for electronic signal cables

and one high quality ground. The signal conduits lead to a separate monitoring booth. A closed circuit television camera is to be installed on the overhead operative light.

Completion of this new cardiothoracic operating room is scheduled for the fall, 1970

D-2. Design of an Intensive Care Unit for Cardiothoracic Surgery

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R. E. Clark, M.D., Surgery
J. A. Collins, M.D., Surgery
J. R. Cox, Jr., BCL
R. W. Hagen, BCL
F. M. Nolle, BCL
L. J. Thomas, M.D., Anesthesiology
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Support: RR 00396
HE 00082
HE 11233
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Missouri Heart Association
Washington University
Barnes Hospital

The design of an intensive care unit (ICU) for cardiothoracic surgery at Barnes Hospital was initiated in the spring of 1970 and is continuing to evolve. BCL has collaborated with the Department of Surgery in the planning of the physical configuration, environmental control and human engineering for the ICU, as well as the monitoring, processing and displaying of patient data. The design to date is the result of numerous meetings, conferences and discussions involving physicians, nurses, manufacturer's representatives and BCL personnel, in addition to visits to existing ICU's, reviews of the literature and experience. The overriding goal of this design is to improve the care of patients undergoing cardiothoracic surgery and to demonstrate this improved care in the renovated ICU.

The first series of meetings was concerned with establishing a set of basic design criteria acceptable to all. The resulting criteria dictates a practical design specifically suited to the needs of the patients and staff of Barnes Hospital.

The following is a partial list of the basic design goals.

1) Permit monitored patient data to be displayed at the patient's bedside.

2) Permit one nurse to simultaneously provide routine care in a particular patient's room while monitoring the basic data of any patient in the ICU.

3) Permit a nurse to detect a patient emergency rapidly from any point in the ICU.

4) Permit a nurse to observe all patient beds, readily scan the basic data from all patients and carry out a substantial portion of her routine charting while at the central nurse's station.

5) Automatically generate a reliable history of the basic variables for each patient.

6) Allow for an area within the ICU and away from the patients where the patient's current and historical data can be intensively reviewed and professionally discussed.

7) Optimize the ICU floor plan including patient rooms, a medication preparation area, monitor console location, storage areas, a doctor's discussion area and a dirty area.

8) Consider the psychological aspects of the patient's environment.

9) Throughout the design emphasize considerations related to human engineering for the ICU activities of the nurses and doctors.

10) The monitoring and display system shall, when complete, permit the display of each patient's heart rate, respiration rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, mean central venous pressure, peak inspired airway pressure, tidal volume and temperature on a selectable digital display while displaying ECG and arterial blood pressure as analog waveforms.

11) Design a monitoring and displaying system that is reliable, employs current technology, is adaptable to advances in transducer technology, and is expandable to the complete monitoring capability described above.

12) Maintain patient and personnel safety in all design.

13) Meet the design goals at minimum cost.

The area of the proposed renovation is located on the second floor of the Rand-Johnson building. Study revealed that the available floor

space, with an addition of about 20% in area, can support four partitioned patient rooms. The proposed floor plan is a result of observing the movement of personnel in the existing ICU, experience and review of the literature. Work is continuing on detailed mechanical design and layout.

The patient's physiological condition is to be monitored via commercially available transducers and associated amplifiers. These amplifiers will be contained in an instrumentation island located near the patient bed. Initially the instrumentation will monitor ECG, arterial blood pressure, central venous pressure, inspired airway pressure, respiratory air flow and temperature for each patient. Analog displays of ECG and arterial blood pressure for each patient will be presented on a conventional dual trace oscilloscope located at that patient's bedside. All monitored signals will be carried to a small digital computer system.

The functions of the digital computer system are to perform analog-to-digital conversion on patient signals, calculate derived data from the primary patient signals, generate the data for driving the ICU display system, compare patient data with assigned limits and act as a preprocessor for a larger computer located remotely. A "hard copy" patient history will be generated through the remote computer system.

The proposed display system includes digital displays, CCTV monitors and patient alarm indicators. Each patient room will contain two displays which enable a nurse to observe any ICU patient's ECG and arterial blood pressure waveform on a CCTV monitor as well as select any one of that patient's monitored parameters for viewing on a digital display.

The central nurses' station has one monitor and selectable digital readout panel for each patient in the ICU together with a two channel thermal recorder for recording patient waveforms. Alarm condition indicators are located at the entrance to each patient's room. The doctor's discussion station has one CCTV monitor for each patient, a selectable digital display and a two channel thermal recorder. The design of the monitoring, processing and display system is continuing.

D-3. Heart Pump Rate and Duty Cycle Control

Personnel: P. S. Berger, BCL
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Support: RR 00396
Washington University

In the treatment of heart failure due to myocardial infarction a common practice is to introduce assistive devices in order to relax the

failing left ventricle. Counterpulsation techniques serve to provide partial cardiac bypass thus rendering relaxation to the left ventricle while at the same time providing sufficient blood flow to the heart muscle.

A Sarns, Inc. mean flow roller pump was converted to a pulsatile pump by means of a switching circuit for the applied line voltage. By adjusting the controls, the pulse rate was variable from 60 to 120 beats per minute and the systole/diastole ratio was variable from 0.4 to 1.0 (i.e., systolic duty cycle variable from 30% to 50%). Once the systolic duty cycle is set, the pumping rate can be adjusted independently and the control will maintain the preset systolic duty cycle.

The pump is provided with a resettable digital counter which can be used to measure blood volume passed by the pump over an interval from one pulse to several days of pulsatile pumping.

No modification of the internal pump mechanism was necessary and the pump may be switched from the pulsatile mode to the mean flow mode for which it was originally designed.

D-4. A Tachometer Sensor for Life Tests of a Prosthetic Heart Valve

Personnel: P. S. Berger, BCL
R. E. Clark, M.D., Surgery

Support: RR 00396
Washington University

A tachometer sensor is a device which converts shaft rotation to an integral number of pulses by sensing the number of times a shaft-mounted magnet passes a pickup coil located near the shaft. The sensor drives a saturating amplifier which provides a square pulse train input to a HP5245L counter to give shaft rotation rate in revolutions per second. The amplifier is located on a small circuit card. By knowing the pumping rate determined by the tachometer attached to the pump shaft, the amount of fluid passing through the valves can be determined.

D-5. Cardiac Catheterization Laboratory Computer System

Personnel: J. M. Pexa, BCL
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G. C. Oliver, M.D., Medicine

Support: RR 00396
HE 11233
Missouri Heart Association

The computer system for the catheterization laboratory has been described previously (PR 5, C-8). A Vuetech Multifocus projection device has been added to the system to facilitate ventricular volume studies. The apparatus provides for the projection of 35mm cineangiograms on a desk level ground glass screen so that tracing can be done using a Rho-Theta Position Transducer.

D-6. Cardiac Catheterization Laboratory Software

Personnel: W. V. Glenn, Jr., BCL
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The PC programs for analyzing cardiac catheterization data as reported in PR 5, C-9 were expanded and rewritten in order to run from cassette tape units (see F-15). The revised system is described in BCL Monographs 133 and 134. Specific tasks which software has been prepared are:

1) Gather and store intravascular pressure tracings using variable sampling rates on three simultaneous analog channels.

2) Compute from pressure data such parameters as end diastolic pressure, maximum systolic pressure, dicrotic notch pressure, valve opening and closing pressures, mean pressures, systolic ejection period, diastolic filling period, maximum dP/dt, valve gradients, valve flows, and valve areas.

3) Gather and store dye dilution curves.

4) Compute from dye curves the appearance time, build-up time, mean transit time, and cardiac output (based on exponential curve fitting of the downslope in the dye curve).

5) Calculation of cardiac output and stroke volume from aortic pressure tracings.

6) Calculation of left ventricular volume from single plane left ventricular cineangiograms (taken at 50 frames/second) in order to construct pressure-volume hysteresis loops on the oscilloscope screen and to quantify mitral or aortic valve regurgitation.

7) Output raw data and resulting calculations on either a digital plotter or an oscilloscope screen.

8) Keyboard entry of patient data (name, age, sex, etc.), and other off-line data such as pH, PO_2, oxygen saturation, etc., of various chambers.

9) Teletype summary of important results from each catheterization procedure.

When the above programs are fully operational, effort will proceed on simple routines for permanent storage (on IBM 360/50) of patient information, raw data, and calculations.

E. Collaborative Data Processing

The reports presented below describe current work on our computer network with the IBM 360/50 at the hub and ten Programmed Consoles and LINC's at the periphery. These small computers gather, preprocess and display data while the IBM 360/50 maintains files and carries out complex numerical processing.

E-1. Teleprocessing Programs

Personnel: E. Van Patten

Support: RR 00396

The teleprocessing programs for Collaborative Data Processing have been in operation now for more than a year. Revisions and expansions have been required and can be divided according to whether the communication programs run in the IBM 360/50, the LINC or the PC.

IBM 360/50 Communications. The use of LINC's and PC's as remote terminals of the IBM 360/50 has increased over the past year necessitating the addition of two more data lines. Basically the programs are the same as they were (see PR 5, E-3), but the need for a few changes became obvious with the experience of usage by others. The adoption of Release 17 of the IBM 360 Operating System (OS) in September, 1969 also produced a requirement for revisions.

The most significant changes have been to the error handling routine in the 360 program. In Release 17 the flagging of some errors from the IBM 2701 (the interface between the data lines and the 360) was changed, so that some errors slipped through and were handled by standard OS routines. Such errors do not allow automatic recovery and many jobs were unnecessarily being abnormally terminated. This situation has been corrected, so that all except hardware failures allow continuation of the job.

Of course, two different simultaneous requests to write on a file would cause problems were it not the "BZ" response included in the original system. It has been discovered that an attempt to delete that occurs simultaneously with an attempt to write on the same file can cause the same kind of interference, and resultant file destruction. Since the request to write on the file can come from any other data line or the batch partition itself, the interference is not under the user's control. The delete module has, therefore, been changed to include checking the list of files currently in use, and a "BZ" response to a delete request will now be received when the file is busy.

A COPY function has been added, which duplicates a member of a file, in the same file, or in another file, leaving the original member intact.

This is part of GTPT. This module has been further altered to signal the end of the member in the GET portion of GTPT by a record of zero length rather than by sending an EOT (end of transmission). This use of EOT made it difficult to be sure when the 360 was in the idle state. This revision of the protocol makes the whole procedure simpler.

The RUN module was rewritten to comply with the requirements of HASP II, Version 2 which was put into operation in February of this year. The method of inserting jobs into the input stream for batch processing in the 360 was simplified from the method used with the previous versions of HASP. It is now equivalent to writing on a file.

Most of the modules have been changed so that when a job is terminated because of an error, the source of the error (disc, data line, read, or write) is identified. This was particularly beneficial in revising the error handling appendage. Further, after a return to the monitor as a result of an error, the "CAN" character is sent repetitively until some other action occurs on that data line. Previously just a single CAN was sent and it frequently was not received by the terminal.

LINC Communications. The LINC uses its relay register in transmitting to the 360; the same register is used to operate the teletype, and other peripheral devices. A hardware change was made to the LINC to make the bit used for communications independent of other uses. The communications subroutine was revised to accord with this change (See BCL Monograph 112).

PC Communications. The PC utility routine, the communications monitor and the revised PC communications subroutine have been in full operation for over six months. BCL Monograph 95, "Using the PC-360 Communications" describes these routines in detail.

E-2. LINC Program to Backup IBM 360/50 Disc Files

Personnel: E. Van Patten, BCL

Support: RR 00396

Disc failures that destroy files or make them unreachable are rare, but they can happen. Currently, disc files are copied to magnetic tape periodically, against a possible need to reconstitute them. This method, however, does not give the PC or LINC user of such files sufficient control either over which members of a file should be saved, or just when vital data should have a backup copy.

A system is under development for copying 360 disc files to LINC tape, and for restoring disc files from LINC tape. This is an independent system (it does not operate under LAP6) so that all but a about 10 blocks of a LINC tape are available for file storage. Selection of the backup program or the restore program is made via the initial display, as well as the choice of copying an entire file or just selected members. If the latter, the names of the members are printed on the teletype and acceptance or rejection is signified by striking the appropriate key on the LINC keyboard. If the complete file is to be copied the operation proceeds without interruption unless more than one LINC tape is required. It is estimated that 35 tracks of 360 disc data will be contained on one LINC tape, so more than one tape could well be needed to preserve a file.

Similarly, the contents of a tape may be returned to the 360 disc either in total, or by selecting members. The program will also provide a teletype listing of the members of any 360 disc file, or the members stored on a tape.

A specialized communications routine has been written for this package. It does no conversion, but stores the 7-bit ASCII characters as received, packing three characters (21 bits) into two LINC words (24 bits). End-of-record marks are employed to allow the maximum utilization of the tape.

It is hoped that this program, which is in the checkout phase, will prove a convenience and a safeguard to users of the 360 communications with either a PC or a LINC.

E-3. General Purpose Analog Input System; PC to IBM 360/50

Personnel: J. A. Parker, BCL
W. F. Holmes, BCL

Support: RR 00396

A PC program, SAMPLE, was developed for general purpose signal sampling and input to the IBM 360/50. Up to 4 channels of analog data may be sampled simultaneously at a rate specified by the user. An oscilliscope display and a CalComp Digital Plotter aid in viewing the sampled data. The digitized data may subsequently be sent to the IBM 360/50 disc, where it is readily available to FORTRAN programs. Character data may be interspersed with the converted analog data.

E-4. General Purpose Graphic Input System; PC to IBM 360/50

Personnel: J. A. Parker, BCL
W. F. Holmes, BCL

Support: RR 00396

A PC program, DRAW, was developed for general purpose graphic input to the IBM 360/50 using the Rho-Theta Position Transducer (BCL Monograph 139). Graphic data (line segments and points) traced by the Rho-Theta are digitized in a cartesian coordinate system defined by the user. As the tracing proceeds, the digitized data are displayed on the storage oscilliscope. The digitized data may be plotted on the Calcomp Digital Plotter allowing a check on the accuracy of the tracing and digitizing procedure. These data may subsequently be transmitted to the IBM 360/50 disc, where they are readily available to FORTRAN programs. Character data, typed in at the PC keyboard may be interspersed with the converted Rho-Theta data. DRAW has been specially written so that it is easily modifiable for a variety of special purposes.

DRAW brings together and relies heavily on four previously developed programs: PC-360 communications subroutine (BCL Monograph 95), RHOTHETA (BCL Monograph 55), PLOT (BCL Monograph 68), and PCQ&A (BCL Monograph 127).

E-5. Installation of Sangamo T201B Modems for the IBM 2780

Personnel: V. W. Gerth, Jr., BCL

Support: RR 00396

The installation of an IBM 2780 remote card reader/printer required a 2400 bps data link between BCL and the Information Processing Center. Purchased data sets were used along with line leased from Southwestern Bell Telephone Company. The data sets are Sangamo T201B units utilizing a 4-wire full duplex C2 conditioned line. The data lines were routed through the existing BCL data communication facility to provide flexibility and cross patching in case of failures.

E-6. Switching System for Collaborative Data Processing

Personnel: G. J. Blaine
H. D. Ambos

Support: RR 00396

The switching system permits up to 30 remote terminals (presently 10) to gain access on a first-come, first-served basis to one of four

communication channels (BCL Monograph 123). After operation for a period of 6-8 months reliability problems were experienced. The crossbar auxiliary contacts were utilized to provide a mechanical delay for a timing pulse during line selection. An investigation disclosed that contact impedance increased substantially after many operations. An engineering modification was installed which eliminates the relay contacts in the delay circuit and substitutes a one-shot multi-vibrator. No further difficulty has been experienced.

E-7. Switching System Detector for Collaborative Data Processing

Personnel: P. Berger, BCL
H. D. Ambos, BCL

Support: RR 00396

In order to verify whether or not data lines are available to peripheral computers from the IBM 2701 terminal on the main university campus, a detector circuit was constructed and connected to a Rustrak 200 series recorder. The presence of a "carrier" signal from the IBM 2701 terminal is detected and converted to a dc level which is used to drive the pen recorder. In this way, a permanent record of all times the system is available can be obtained.

E-8. Design Studies for a Data Concentrator

Personnel: A. Ichijo, BCL

Support: RR 00396

Initial design studies have been carried out on a data concentrator system to replace the present IBM 2701 units. Plans call for accommodation of ten to twenty, 1200-baud, start-stop communication channels. Early results indicate that a system using a small computer such as the PDP-11 is less expensive than any of the commercially available data concentrators. Our studies included the IBM 2701, 2702, and 2703 as well as the Varian 520/DC, Tempo and Tec 520 PCP systems.

F. Other Applications of Computers

Computer applications not appropriate for the previous five sections are reported in this section. A few supporting activities are also described. As in many of the preceding sections, much of the work depends upon collaboration with our colleagues. Their names and any associated financial support are listed at the beginning of each report.

F-1. A Mass Spectrometer Data Acquisition System

Personnel: W. F. Holmes, BCL
W. H. Holland, Psychiatry
J. A. Parker, BCL

Support: RR 00396
CA 10926
GM 28163
NB 05159

Development of a computerized system for mass spectroscopy is underway utilizing a PDP-12 computer. The first phase comprises the design of a data acquisition system for the Medical School's LKB-9000 gas chromatograph-mass spectrometer. While the work is not yet finished, it is apparent that it will soon be possible to acquire routinely large numbers of mass spectra in computerized form. The next phase of work will concentrate on utilizing the abundance of reduced data through interactive programs involving the experimenter. The system will be largely independent of the mass spectrometer, and can be used with any PDP-12. Adaption to other mass spectrometers will only require modifications to the interface with the PDP-12, and to the basic programs controlling raw data input.

An interface has been constructed for starting the mass spectrometer scan, sensing the "scan done" condition, registering mass marking pulses, and sampling the mass abundance data. The 10-bit A-D converter of the PDP-12 is made to cover a 13-bit range (1:8000) of mass abundance by using two channels with a 1:8 gain ratio, with an error of less than 1% at the transition between them. A third channel may be added to extend the range to 1:64,000, which is well beyond the range of the galvonometer recording system presently used. A generalized file system for magnetic tape storage, retrieval, display, and plotting has been developed, which is now fully operational for digitized raw data. A mass peak detection algorithm has been tested using raw data displays, and is now being used to display data in a partially reduced form where only mass abundance peaks are retained, with a great reduction

in the amount of data required. Using this peak data, about 150 scans of 250 mass peaks each can be stored on one LINC tape, allowing continual scanning throughout a gas chromatography run. By this method all peaks in the run are routinely available for positive identification. Overlapping chromatograph peaks can often be separated by examining appropriate mass values unique for each unseparated compound.

Further processing of peak data to a reduced form requires assignment of mass values to each peak using a calibration table. Preliminary results indicate that the mass spectrometer is stable enough for on-line reduction of a continually scanned chromatograph run (about 500 scans/tape), but further use must bear this out. Each form of data, raw, peak, and reduced has its special uses. Raw data from rapid repetitive scans can be readily averaged to obtain detection levels impossible with the galvonometer recorders. Many partially resolved mass abundance peaks have been observed which could be separated with off-line deconvolution techniques applied to the raw data. The peak data still retain fractional mass information which can narrow the possible range of atomic formulae having the same nominal mass value when rounded to an integer mass. Reduced data, containing only integer masses, half masses, and metastable peaks, will be used for further data manipulations, such as compound identification, separation of unresolved gas chromatograph peaks, quantitative analysis, and studies on biochemical pathways using stable isotopes as tracers.

Publications:

Holmes, W. F., "Low Resolution Mass Spectrometers," (Part of Chapter II, "Mass Spectrometer Data Acquisition and Processing Systems") in Biochemical Applications of Mass Spectroscopy, G. Waller, editor, in press. (BCL Monograph 137)

F-2. LINC Calculation of the Isotope Dispersion of a Molecular Fragment in the Mass Spectrometer

Personnel: J. A. Parker, BCL
W. F. Holmes, BCL

Support: RR 00396
Washington University

A preliminary version of a LINC program was developed to calculate the isotope dispersion mass spectrum of a single molecular fragment, given the formula and the abundances of isotopes of the various elements

in the fragment. The problem encountered with an exact calculation of a mass spectrum was that for even relatively small fragments the length of time required was unacceptable. An approximate algorithm for such small fragments was developed and running times are reasonable.

F-3. Analysis of Sedimentation Equilibrium Scans from an Ultracentrifuge

Personnel: J. A. Parker, BCL
W. F. Holmes, BCL

Support: RR 00396

Measurement of molecular weights by the sedimentation equilibrium method is a standard biochemical procedure. The Biochemistry Department maintains a Spinco Model E Ultracentrifuge with a scanning ultraviolet densitometer. The output appears on a strip chart recorder as a curve representing optical density versus distance from the centrifuge rotor, plus an internally generated calibration curve. Although numerous scans can be recorded during a sedimentation equilibrium run, each scan requires several hours of calculations to compute a molecular weight. While the basic formula for the molecular weight is quite simple, it assumes ideal conditions seldom realized in practice. Thus a number of runs under varying experimental conditions, and a number of scans for each run are desirable for a thorough study.

The Rho-Theta data acquisition system (see E-4) has been used to trace the recorder curves from each scan into the PC, digitizing the data and sending it to the IBM 360/50. Auxiliary information such as temperature and protein density is sent using a Questions and Answers display tailored to sedimentation equilibrium analysis. The data are processed by a FORTRAN program residing in the 360. The slope of logarithm of the optical density versus the square of the distance from the rotor is determined by a least squares fitting procedure, and used to calculate the molecular weight.

The results are sent to a remote high speed printer located in the Medical School. They consist of a plot of the digitized recorder curves with the auxiliary information plus a plot of the reduced data, nominally a straight line, along with the best least squares fit. Since the data often do not provide a good fit over their entire extent, the user can select a number of pairs of points on each scan between which the data will be fit.

F-4. Time Sharing Terminal

Personnel: W. F. Holmes, BCL

Support: RR 00396
Washington University

A teletypewriter, connected by a dialup telephone line to a General Electric 265 time sharing computer, continued operation in the Biochemistry Department (see PR 5, F-1). Limited support was provided to qualified users as a supplement to the laboratory's communication system between the University's IBM 360/50 and the PC and LINC. Partly as a consequence of experience with the time sharing terminal, a PDP-12 computer has been installed in the Biochemistry Department. It will handle high volume raw data applications unsuitable for teletype input, as well as simple interactive calculations in the FOCAL language, which is similar to the BASIC and FORTRAN languages used on the GE computer. The time sharing terminal will be retained under the support of the Biochemistry Department for larger and lengthier interactive calculations, beyond the range of FOCAL. Several new programs developed by Biochemistry personnel are listed in the following three reports.

F-5. Analysis of First Order Kinetic Data

Personnel: S. Garavelli, Biochemistry

Support: RR 00396
AM 1332
GB 8074
Washington University

A simple program was set up to calculate pseudo first order rate constants from data presumed to fit a decaying exponential curve. A least square fit is calculated of the best straight line passing through the logarithm of the raw data. Limits may be set for rejection of data points. If such points are found, the new fit is calculated without them. The process continues until all points fit within the range selected. The final output is a plot of the data with an indication of those points rejected during the fitting.

F-6. Molecular Orbital Calculations for Trinitrobenzenesulfonate

Personnel: D. Bates, Biochemistry

Support: RR 00396
Washington University

In the course of studying the possible ways in which trinitrobenzenesulfonate can stack with the reduced nicotinamide portion of the coenzyme DPHN (reduced diphosphopyridine nucleotide), electronic restrictions were introduced into the steric model. To do this, a set of programs was written which would solve the molecular orbital determinant of the simple Huckel approach to molecular orbitals. The programs are applicable to any case up to 20 atoms. They calculate energy levels, molecular orbital coefficients, total π electron density at each atom, and partial mobile bond order. The electron densities were then used to rule out some of the possibilities of stacking that were allowed sterically.

F-7. Sedimentation Analysis of a Multiple-peak Reversibly Polymerizing System in the Ultracentrifuge

Personnel: R. Aaronson, Biochemistry

Support: RR 00396
Washington University

The association-dissociation behavior of certain enzymes has been implicated in their control function. Analysis of the mechanism of reversible polymerization of one such enzyme, PFK, reveals an apparent anomaly. Schlieren patterns of sedimentation of PFK in the ultracentrifuge indicate the presence of at least three species in equilibrium. Calculations of the observed sedimentation coefficients and concentrations under various conditions were necessary for comparison with simulations based on several models of reversibly associating systems in an attempt to elucidate the mode of polymerization.

F-8. Spectrum of Chirps

Personnel: I. Nabelek, Central Institute for the Deaf
A. Nabelek, Central Institute for the Deaf
I. J. Hirsh, Central Institute for the Deaf
J. Markham, BCL
P. Handler, CSL

Support: RR 00396
NS 03856

This project studied the pitch-perception of frequency glides. It was found that the pitch of a short sound burst with a large frequency difference between the final and initial frequencies Δf or of longer bursts with smaller frequency difference, was judged as being close to the pitch of a burst with a frequency equal to the arithmetic mean frequency of the burst. The standard deviations of these judgments were small. However, judgments occurred with large dispersions and/or their means moved away from the arithmetic mean frequency when the product K of the burst duration T and frequency difference Δf was larger than 5. The change in the character of judgments corresponds to the change of the power spectra of bursts from a spectrum with one maximum to one with many maxima. Spectra of bursts with frequency glides were calculated on a LINC using a Fast-Fourier-Transform program. Several bursts were analyzed also on the IBM 360/50 computer based on formulas given in Papoulis[1]. The methods yielded two different results and careful review of both techniques disclosed that the differences were caused by an error in Papoulis.

(1) A. Papoulis, The Fourier Integral and its Applications, McGraw-Hill, New York, 1962.

Abstracts:

I. Nabelek, A. Nabelek and I. J. Hirsh. "Pitch Perception of Two Types of Frequency Change: Glides and Jumps," Journal of the Acoustical Society of America, Vol. 47, No. 1, Part 1, p. 118. January, 1970. Presented at the 78th Meeting of the Acoustical Society of America in San Diego, California, November, 1969.

I. Nabelek and A. Nabelek. "Frequency Glides -- Their Spectra and Pitch Perception," Journal of the Acoustical Society of America, Vol. 47, No. 1, Part 1, p. 119. January, 1970. Presented at the 78th Meeting of the Acoustical Society of America in San Diego, California, November, 1969.

Publications:

I. Nabelek, A. Nabelek, and I. J. Hirsh. "Pitch of Tone Bursts of Changing Frequency," Journal of the Acoustical Society of America, 47: 8, 1970.

F-9 Payoff Matrices for Confidence Rating Experiments

Personnel: D. L. Snyder, BCL
C. S. Watson, Ph.D., Central Institute for the Deaf
D. A. Ronken, Ph.D., Central Institute for the Deaf

Support: RR 00396
NS 03856

Several solutions are available for the optimum behavior of a human observer stimulated by noisy information in a binary hypothesis testing task. A useful solution is obtained by assuming that the observer acts to maximize the expected payoff given the a priori probabilities of the hypotheses and the two-by-two payoff matrix. An analogous solution for the confidence-rating (i.e., binary hypotheses with m-rated decisions) experiment[1] has not appeared in the literature. Such a solution has been obtained[2], and has been compared with the performance of observers in auditory discrimination experiments. As in the case of binary decisions, the conformity of actual observers to the optimum behavior of the model is less than complete. The decision rules of the model yield identical optimum behavior for payoff matrices that are quite different. We thus suspect that human observers will have considerable difficulty in matching the ideal behavior.

(1) J. P. Egan, A. I. Schulman, and G. Z. Greenberg, "Operating Characteristics Determined by Binary Decisions and Ratings," Journal of the Acoustical Society of America, 31: 6, 1969.

(2) D. L. Snyder, "Binary Hypothesis Testing Using Rated Decisions," BCL, private correspondence; December, 1969.

F-10. Analysis of Pulmonary Blood Flow as a Function of Cyclic Lung Inflation

Personnel: L. J. Thomas, M.D., Anesthesiology
A. Roos, M.D., Anesthesiology
S. Sutera, Ph.D., Mechanical Engineering
V. Luthra, Mechanical Engineering

Support: RR 00396
HE 00082
HE 10523
Washington University

The cyclic blood flow response to sinusoidal lung inflation over a wide range of frequencies has been studied under various inflation conditions with a DC perfusion source in excised cat lungs (see PR 5, F-20).

Total lung compliance and resistance (airway plus tissue) as well as mean vascular conductance are calculated from the data. Examination of the data has led to the conclusion that postitive pressure inflation involves a primarily resistive coupling between inflation pressure and blood flow whereas negative pressure inflation involves a significant capacitive component, assuming a small inductive reactance at these low frequencies.

The observations have been synthesized with existing knowledge of the physical relations between the air spaces and vasculature of the lung in the form of a simple model of the system which has been solved by the perturbation technique and then programmed on the LINC computer for study of model behavior. When knowledge or reasonable estimates of the appropriate lung parameters are substituted into the model it shows behavior remarkably similar to that of the isolated lung preparations. Manuscripts are now in preparation for publication.

F-11. Calculation of Aldosterone Secretion Rates

Personnel: M. L. Rockoff, BCL
V. V. Weldon, M.D., Pediatrics

Support: RR 00396
HD 04014
Washington University

A program was written for the SCM Cogito 1016PR to calculate the aldosterone secretion rate of a patient according to the method proposed by Kliman and Peterson[1], and modified by Finkelstein, et al[2]. The data are obtained from 24 hour urine samples on patients with various endocrinopathies.

[1] Kliman, B. and Peterson, R. E., "Double Isotope Derivative Assay of Aldosterone in Biological Extracts," J. Biol. Chem., 235: 1639, 1960.

[2] Finkelstein, J. W., Kowarski, A., Spaulding, J. S. and Migeon, C. J., "Effects of Various Preparations of Human Growth Hormone on Aldosterone Secretion Rate of Hypopituitary Dwarfs," Amer. J. Med., 38: 517, 1965.

F-12. Sodium Transport in the Toad Bladder

Personnel: M. L. Rockoff, BCL
A. L. Finn, M.D., Yale University

Support: RR 00396
AM 10025

A compartmental model of toad bladder sodium content has been developed, continuing the work described last year (see PR 5, F-10). The model has two tissue compartments, one of which acts as the transport pool and communicates directly with the serosal and mucosal bathing media. The second tissue compartment does not respond to physiological perturbations and is considered not to communicate with the transport pool. With this model it is possible to calculate the four unidirectional fluxes across the opposite faces of the transport compartment, as well as the amount of sodium in the compartment. The model has been selected as being the simplest one which is consistent with data obtained by the following physiological perturbations: antidiuretic hormone (ADH), amphotericin B, and oubaine have been added to the medium; the sodium concentration of the loading solution has been changed; the temperature has been changed; and lastly, the transepithelial electrical potential has been changed. It has been shown that ADH affects the transport pool on two separate sites. In the first place, the hormone stimulates entry at the mucosal side of the transport compartment, increasing the pool size. Second, it has a distinct stimulatory effect on the rate coefficient for efflux across the serosal boundary, the pump rate coefficient.

Publications:

Finn, A. L. and Rockoff, M. L., "The Kinetics of Sodium Transport in the Toad Bladder, I. Determination of the Transport Pool." Submitted for publication.

Finn, A. L., "The Kinetics of Sodium Transport in the Toad Bladder, II. Dual Effects of Vasopressin." Submitted for publication.

F-13. Interactive Modeling

Personnel: M. L. Rockoff, BCL
J. Markham, BCL
D. Kaplan, BCL

Support: RR 00396
Washington University

The development of a PC/360 facility for interactively building a mathematical model of a physiological system (see PR 5, E-6) has continued.

The Simulation, Analysis and Modeling program (SAAM) developed by Berman has been used extensively (see F-12 and C-10) this year. Since the installation of the IBM 2780 remote terminal, it has been possible to obtain more satisfactory output from a PC-submitted SAAM run by using the terminal printer instead of the Motorola Printer.

Investigation of the "condition" of a curve fitting problem has continued and some results have been presented[1]. The problem is to fit observations (data) $y_1,\ldots y_N$ obtained at times $t_1,\ldots,t_N$ to a function of the form

$$f(t,\theta,\ldots,\theta_{2m}) = f(t,\theta) = \sum_{i=1}^{m} \theta_{2i-1}\, e^{-\theta_{2i} t} .$$

The condition of the problem is studied through the use of the matrix

$$M_{ij}\ (t_1,\ldots,t_N,\theta) = \sum_{k=1}^{N} \omega_k \frac{\partial f(t_k,\theta)}{\partial \theta_i} \frac{\partial f(t_k,\theta)}{\partial \theta_j}$$

If the observations are of the form

$$y_k = f(t_k,\theta_0) + \varepsilon_k$$

where θ_0 is some true, fixed parameter vector and the ε_k are independent random normal deviates with mean zero and variances $\frac{1}{\omega_k}$, then $M(t_1,\ldots,t_N,\theta_0)$ is the Fisher (or differential) information matrix[2] associated with maximum likelihood estimation for the parameter vector θ. The inverse M^{-1} is a lower bound on the variance-covariance matrix that would be obtained if the indicated experiment were actually performed. Hence, if one knows the parameter vector θ_0 approximately, one can study the effects of changes in the observation times t_k and variances $\frac{1}{\omega_k}$ before the experiment is performed.

Because the exponential fitting problem is known to be poorly conditioned[3,4], i.e., that given observations can be fit by functions with widely different parameters, it was decided to see if this problem could be replaced in some physiological situations with a better conditioned problem. Specifically, in washout studies in brain and other organs such as the lung, when the data are fit as shown in the first equation above,

the coefficient θ_{2i-1} is interpreted to be the volume of a "compartment" being washed out at a rate proportional to θ_{2i}. Kety[5] and Reivich[6] have proposed that the washout curve be regarded as made up of a continuum of compartments instead of two. Turner[7] proposed that this continuum be described by one or more gamma distribution; we have studied this situation. For each of four underlying distributions (three gamma distributions and the sum of two such distributions) we generated the following "washout data": two sums of 10 exponentials, the sum of 20 exponentials and the integral of the complete spectrum of exponentials. We found that for early values of time the four curves generated from the same underlying distribution produced nearly the same washout; the presence of smaller exponentials (corresponding to slowly washed out compartments) produced differences in the washout at later times.

Also we found that, to the eye, the data appear to be generated by a sum of two exponentials, regardless of which model has been used to generate the data. This result bears on the work of Reivich[6] who constructed "washout data" from a model consisting of the sum of two Gaussian distributions. Our results suggest that many mathematical models will generate data compatible with a two-exponential model.

We plan to fit data from a series of patients to see whether the parameters of the underlying gamma distribution (or functions of them such as the moments of the distribution) correlate reliably with clinical findings.

(1) Rockoff, M. L., "Fitting Data with Linear Combinations of Exponentials," presented at the Society for Industrial and Applied Mathematics 1970 National Meeting, June 30, 1970.

(2) Savage, L. J., The Foundations of Statistics, Wiley, N. Y., 1954, p236.

(3) Servais, Fr. J., "On the Expansion of Experimental Functions in Series of Descending Exponentials of Real Argument," Nucl. Sci. Eng., 34: 196 1968.

(4) Lanczos, C., Applied Analysis, Prentice-Hall, 1956.

(5) Kety, S. S., "Observations on the Validity of a Two Compartmental Model of the Cerebral Circulation," in Regional Cerebral Blood Flow, Ed. Ingvar, D. H., and Lassen, N. A., Acta Neurol. Scand., Supp. 14, 1965, p. 85.

(6) Reivich, M., Slater, R. and Sand, N., "Further Studies on Exponential Models of Cerebral Clearance Curves," in Cerebral Blood Flow, Ed. Brock, M., et al, Springer-Verlag, 1969.

(7) Turner, M. E., "The Spectrum of a Linear Network: A Simple Approach to the n Compartment Problem," Biometrics, 20: 827, 1964.

F-14. Mathematical Models of the Mechanics of the Cochlea

Personnel: M. D. Lien, BCL
J. R. Cox, Jr., BCL

Support: RR 00396

As a continuation of the work described in PR 4, F-6, the cochlea is treated as a time-invariant linear system with the displacement of the stapes footplate as the input force, and the displacement of a section of the basilar membrane as the output response. Through the fluid in the cochlea, the motion of the membrane interacts with all parts of the membrane.

An integro-differential equation, which describes the combined fluid and membrane motion in the cochlea has been rederived (see PR 4, F-6). Previously the derivation included consideration of the input force, the interacting sources along the membrane, and the longitudinal coupling between adjacent parts of the membrane. The present derivation includes, in addition, the effects of the fluid viscosity and the variation of the membrane thickness. The addition of the effect of viscosity introduces a small change in the expression within the integration sign, and the reconsideration of the membrane mechanics yields a substantially more complex structure for the differential part of the equation.

By methods parallel to the state variable approach to the solution of the Fredholm integral equation, the resulting integro-differential equation has been converted into a set of two simultaneous sixth order differential equations plus a set of boundary conditions. Through empirical data, such as the microphonic voltage observed in the cochlea (see PR 5, F-21) we are seeking to simplify the equation before computing the solution.

F-15. Development of a Cassette Tape System for the Programmed Console

Personnel: J. M. Pexa, BCL
J. R. Cox, Jr., BCL
V. W. Gerth, BCL
K. L. Kunklemann, BCL
C. R. Fraction, BCL

Support: RR 00396

The use of the PC software system developed for the cardiac catheterization laboratory (see PR 5, C-8 and C-9) illustrated the great need for some form of local mass storage which would be faster and more

convenient to use than the Datamaster unit. The storage problem in this instance was two-fold: a method was needed whereby gathered data could be stored with little delay so that the physician would not be required to interrupt the catheterization procedure, and secondly, programs employing many overlays input through the Datamaster were cumbersome to use. It was decided that a digital cassette magnetic tape unit would be the most economical solution to the above problems.

Because digital cassette transports were new and rapidly developing at the time this project was initiated, the interface was made as general as possible with the characteristics of the cassette transport accommodated by software. Such an approach encourages experimentation with different tape formats, data rates and recording schemes, as well as different tape transports.

Connection of a typical cassette transport to the PC is made through three basic types of signal lines: (1) data lines which carry serial data to and from the transport, (2) control lines which specify commands such as "go/stop," and (3) status lines which indicate particular situations which exist at the transport, such as "end-of-tape." For the cassette transport chosen (Digideck Model 60, International Computer Products), the write data lines can be considered as control lines and the read data lines as status lines.

The interface is driven by two IOT instructions which have the effect of placing each of the control lines in one of two states, and sensing the state of each of the status lines. The IOT 52 instruction places the operand into a special register in the interface. The control lines are driven from this register, which can accommodate a total of twelve lines. The IOT 53 instruction causes the binary signals present on twelve status lines to be stored in the effective address in memory.

The standard 300 foot digital cassette is used in the system. The present format allows for 256 blocks per cassette, with 256 12-bit data words and a check sum in each block. A fixed block number is located at the beginning of each block before the data words. The blocks are numbered sequentially from beginning to end. The cassette routines enable the user to move from one block to another in either direction, and to read from or write into any block. The read/write bit time is 250 microseconds. Guard zones before and after the data zone and an interblock zone increase the read/write block time to 1.2 seconds. A move from one location to another on the tape can be executed at three times the normal read/write speed. Rewind time is approximately 90 seconds.

The routines as developed for use in the cardiac catheterization laboratory are a subset of those that will be available for general use. The complete set of routines will include the following:

READ

WRITE

CHECK

READ GROUP

WRITE/CHECK GROUP

READ SPECIAL

WRITE SPECIAL

INITIALIZE.

The first three routines are concerned with a single 256 word (data) block. The two GROUP routines enable the user to optimize the use of the system by reading or writing a number of blocks in succession. These require less time than a number of successive uses of the READ, WRITE and CHECK instructions by reducing the number of starts and stops. The two SPECIAL instructions are used when it is desired to read or write less than a full block of 256 words. The INITIALIZE routine is needed to rewind the tape and place the cassette starting location into the system software.

In addition to the cassette routines, a MARK program prepares a fresh cassette for use on the system by recording the proper format on the tape including block numbers.

The present system consists of two Digideck transports mounted on a single chassis along with the power supplies and logic to switch the signals to either of the two units. Manual rewind switches are also provided. An evaluation of the system performance remains to be completed.

F-16. A Utility Data Terminal Box for the LINC

Personnel: V. W. Gerth, Jr., BCL
K. L. Kunkelmann, BCL

Support: RR 00396

In routine operation several of our LINC's utilize a fairly standard set of peripherals: the CalComp or Houston Plotter, the Motorola Printer, the Teletype, and IBM 360 data communications. A problem arises when more than two of these need to be used simultaneously since the Data Terminal Frame can only accept two individual interface boxes. Consequently, a Data Terminal Box has been developed which incorporates these interfaces into a single unit. DEC R-Series modules were used which are directly compatible with the LINC logic levels.

F-17. A Solid State Keyboard for the LINC

Personnel: V. W. Gerth, Jr., BCL
C. R. Fraction, BCL

Support: RR 00396

Due to chronic reliability problems with the Soroban mechanical keyboard on the classic LINC, an experimental solid state keyboard has been implemented to allow evaluation of both electronic and human factors. A non-encoded keyboard of the Honeywell Microswitch SSK series was obtained and the keys rearranged to conform to the classic LINC arrangement. An interface to the LINC was developed which is plug-in compatible with the Soroban Keyboard. The interface encodes each solid state switch to provide the proper LINC keyboard code and includes a buffer register to store the code until accepted by the computer. Operator response has been favorable with a few cases of minor adaptation problems due to the absence of the familiar mechanical click of the Soroban Keyboard.

F-18. DUMP for the PC

Personnel: M. D. McDonald, BCL

Support: RR 00396

DUMP is a single card PC program, loadable anywhere, that allows the user to print out via an attached Teletype, the contents of specified core locations in signed or unsigned octal or decimal. DUMP occupies 400_8 words of core and uses index registers 0 through 7 (BCL Monograph 120).

F-19. PC Q&A Monograph

Personnel: M. D. McDonald, BCL

Support: RR 00396

A report (BCL Monograph 127) was issued describing the use of the Questions and Answers (Q&A) subroutine for the PC (see PR 5, A-1). The subroutine was made available on IMP manuscript cards or on LINC tape; listings of both versions were included in the Monograph.

F-20. Teletype Subroutine for the PC (PCTEL)

Personnel: M. D. McDonald, BCL

Support: RR 00396

Subroutines were written for the PC to allow the user to print any PC keyboard character on the Teletype and to cause a carriage return and line feed. The subroutines occupy 27_8 core locations and use five index registers in addition to 0 and 5 (BCL Monograph 135).

F-21. Natural Logarithm and Exponential Subroutines for the LINC LN and EXP)

Personnel: M. D. McDonald, BCL

Support: RR 00396

Most methods for evaluating the logarithm and exponential functions with accuracy are either inordinately slow (e.g., Taylor series expansion) or require, for n digits of precision in the result, n + k digits of precision for certain constants, where k is significantly greater than zero (e.g., polynomial coefficients for Hastings' approximations). The algorithms developed for these subroutines have neither of these drawbacks.

The subroutines were written for the LINC (see BCL Monograph 138) and use the DBLFLT package of double precision floating point subroutines (see BCL Technical Report No. 2).

F-22. Scanner Systems Software Development

Personnel: J. H. Scandrett, Ph.D., Physics
A. R. Zacher, Ph.D., Physics

Support: RR 00396
GM 17386
AT 2089

Our graphics monitor system has been modified in order to compile and assemble new programs quickly and easily. Formerly, it was necessary to send all compilations and assemblies through the regular job stream of the IBM 360/50. With our new system, the Fortran compiler, the machine language assembler, and the linking loader can be invoked within our own job step, eliminating the delays and overhead associated with job initiation. Compiler output can be displayed ten lines at a time on the IBM 2260 alphanumeric display, or 50 lines at a time on a Tektronix 611 storage oscilloscope. The display file can be rolled forward and backward for convenience in examining generated output.

F-23. Tissue Culture Measurements

Personnel: J. H. Scandrett, Ph.D., Physics
A. R. Zacher, Ph.D., Physics
L. J. Tolmach, Ph.D., Radiology

Support: RR 00396
CA 04483
GM 17386
AT 2089

Our cell scanning and sizing algorithm has been applied to a pilot study of automatic scanning of cancer cell colonies. Petri dishes with stained cell colonies are photographed on 35 mm film. The scanning system automatically optimizes the scanning density threshold, automatically centers on the visible field and then scans a 256 by 256 point raster, creating a packed binary core image of the cells. The cell sizing algorithm then systematically counts all cells, forming a histogram of cell areas. Comparisons between automatic dish counts and conventional human scanning are in progress.

F-24. Retinal Cell Dimensions

Personnel: J. H. Scandrett, Ph.D., Physics
J. M. Enoch, Ph.D., Ophthalmology

Support: RR 00396
EY 00204
AT 2089

Infrared interferometric photomicrographs of individual frog retinal cells were taken using an image intensifier. Pictures taken before and after a large exposure of visible light show definite but difficult to measure dimensional changes. The outlines of the cylindrically shaped cells are not seen directly but are inferred from a systematic interruption of the interference fringe pattern.

Cell widths were successfully measured to approximately 5% and show an increase in diameter after visible light exposure. Measurements are now in progress to determine the optical thickness in addition to the physical width. This is done by measuring the fractional fringe shift inside the cell boundary compared to outside fringes.

F-25. Data Processing for a Microspectrophotometer

Personnel: A. L. Bodicky, BCL
J. M. Enoch, Ph.D., Opthalmology
L. Broch, B.S., Opthalmology
B. Milder, M.S., Opthalmology
E. Donnagan, Opthalmology

Support: RR 00396
EY 00204
Washington University

An interface to be used with a microspectrophotometer[1] (a system for the measurement of the transmission of light of varying wave lengths) has been described previously (see PR 5, F-22). The development of the microspectrophotometer itself is now nearing completion and early experiments preliminary to the measurement of the optical transmission of retinal tissue are underway. The interface has undergone initial tests and will be installed when alignment and calibration experiments on the microspectrophotometer are complete.

(1) Enoch, J. M., "Retinal Microspectrophotometer", Journal of Optical Society of America, 56: 833, 1966.

F-26. A System for Automatic Drug Injection

Personnel: L. J. Tolmach, Ph.D., Radiology
B. F. Spenner, BCL
J. C. Georgian, M.S., Mechanical Engineering
J. R. Cox, Jr., BCL

Support: RR 00396
CA 04483

A system has been designed to automatically add and remove solutions from tissue culture (Petri) dishes in which cells grow as adhering monolayers under nutrient medium. The completed system (AUDRI) is expected to facilitate study of the effects of exposing cultured mammalian cells to X-rays, cytotoxic drugs, metabolic inhibitors, and other agents. Initially, application to the determination of retained growth capacity (viability), as measured by colony formation, is contemplated. After processing, the dishes will be removed to an incubator where cells will be allowed to develop into countable colonies (see F-23). For example, loss of viability can be studied as a function of duration of treatment, drug concentration, cell age in the generation cycle, treatment fractionation, or the combination of treatments with two different agents. Minor adaptation will allow the system to be used for measuring synthetic rates, particularly by means

of radioactive precursor incorporation into macromolecules. It should permit more rapid acquisition of more precise data than is possible at present, decrease the need for technical help, and -- most importantly -- facilitate the performance of experiments over a 24 hour period as is necessary when studying age-dependent responses in cells with generation-times of the order of one day.

The system works as follows: 48 pairs of dishes that have been inoculated with suitable numbers of cells are arrayed in a helical configuration (suggested by Professor L. S. Lerman, Vanderbilt University) about a vertical lead screw contained in a thermostated enclosure. A rotary actuator, controlled by a servo amplifier, turns the screw and thereby positions a pair of dishes so as to permit an assembly of small tubes to be lowered precisely into the dish. At preselected times, predetermined volumes of solutions are delivered through the tubes (by means of syringe pumps) to any pair of dishes. A wide range of delivery times and volumes are available and at any subsequent time, the medium may be removed (by suction), the dish rinsed, and fresh medium added. Two different solutions (in addition to medium and buffer) can be administered, and two complete treatment cycles can be carried out on each pair of dishes during a 24 hour period, which is the maximum duration of one experiment.

Operation is controlled by a special purpose computer which is provided with a punched tape input (prepared on a LINC) for each experiment. The special purpose computer is a small, solid state, stored program computer with 8-bit words, but otherwise similar to the L-1 designed by Clark[1]. Programs are overlayed in a 64-word, solid state memory from a loop of punched paper tape. All computer input and output is carefully isolated electrically to provide freedom from sensitivity to the electrical noise generated by the mechanical actuators for the system.

(1) Clark, W. A., "A Functional Description of the L-1 Computer". MIT, Lincoln Laboratory Group, Report 51G-0012, March 1960.

F-27. Analog-to-Digital Conversion for Pulmonary Function Studies

Personnel: V. W. Gerth, Jr., BCL
N. Falvey, B.S., Information Processing Center

Support: RR 00396
HE 10237

Pulmonary function studies carried out on patients before and after neck surgery require analog-to-digital conversion of airway pressure and flow signals recorded on analog magnetic tapes. To determine lung compliance and airway resistance the digitized data are recorded on industry-compatible tape for processing on the IBM 360/50. To accomplish

this task an interface to the LINC was constructed to provide a convenient means of sampling the data at different rates. The interface was constructed using DEC system modules and installed in the same Data Terminal Plug In Unit that houses the analog preamplifiers. Any suitable external time base can be used to establish the sampling rate.

F-28. Division Subroutines

Personnel: M. D. McDonald, BCL

Support: RR 00396

Two fast subroutines for division have been written. The first applies to division of a numerator N by the integers 3, 5, and 9 and utilizes the following series expansion:

$$\frac{N}{2^n + 1} = 2^{-n} \left(N - 2^{-n}N + 2^{-2n}N - 2^{-3n}N + 2^{-4n}N \cdots\right)$$

Clearly, only a few shifts and additions are required to calculate the quotient.

A related division algorithm for numerator N and denominator D less than unity can be expressed as follows:

$$\frac{N}{D} = \frac{N}{1-d} = N \left(1 + d + d^2 + d^3 + d^4 + \ldots\right)$$

where $d = 1-D$ is also less than unity assuring convergence. In fact if $d \leq 1/2$ the terms after d^{15} may be ignored for a 15-bit result. The resulting polynomial in d can be factored so that:

$$\frac{N}{D} = N \left(1+d\right) \left(1+d^2\right) \left(1+d^4\right) \left(1+d^8\right)$$

We note that the products may be calculated iteratively with only three squaring operations and four multiplications.

VI. TRAINING ACTIVITIES

During the year the Biomedical Computer Laboratory engaged in the following training activities:

Course in LINC and PC Programming, November 1969

This course was taught by Michael D. McDonald and included binary arithmetic and coding in both machine language and assembly language. Attending the course were:

Uttamchand Bhanbari, M.S.	EE Graduate Student
Robert S. Bricker, M.D.	Surgery
Robert M. Burton, Jr.	Biology
Franco A. Chakkalakal, M.S.	EE Graduate Student
John O. Eichling, Ph.D.	Radiology
Betty Greenwood	BCL
John D. Halverson, M.D.	Surgery
William Holland, A.B.	Psychiatry
B. Leonard Holman, M.D.	Radiology
Sung Cheng Huang, M.S.	BCL
Aki Ichijo, B.S.	BCL
Duck On Kim, M.S.	EE Graduate Student
Gene Lee, M.S.	EE Graduate Student
Ralph Lehman, M.D.	Neurosurgery
Susan L. Levine, A.B.	Psychiatry
Leo Lopez, B.S.	Radiology
Lamar H. Ochs, M.D.	Pharmacology
Donald S. Quon, B.S.	EE Graduate Student
V. R. Sarma, B.S.	Computer Systems Laboratory
William Sherman, Ph.D.	Psychiatry

Course in LINC and PC Programming, April, 1970

This course was also taught by Michael D. McDonald with the same content as the November course. Attending the course were:

Peter Ansbacher	Space Science Research Center, University of Missouri
Robert Arnzen, Ph.D.	Computer Systems Laboratory, BCL
Luis D. Benitez, M.D.	Central Institute for the Deaf
Philip Berger, M.S.	BCL
Uisik Choi, M.S.	Computer Systems Laboratory
Harold Gene Cohen	Physiology
David Crowley, Ph.D.	Otolaryngology
Nancy Eilers	Physiology

William Hancock, Ph.D.	Biochemistry
Edward Hill	Medical Student
Susan R. Holmes, B.A.	Psychiatry
Steven Iceland, B.A.	Dental Student, BCL
Leonard Jarett, M.D.	Pathology
Judy Lifton	Radiology
Ekkehard Othmer, M.D.	Psychiatry
Robert Parkey	Radiology, University of Missouri
Erol Rauchbach, M.D.	Otolaryngology
Jane Sadell	Biostatistics
D. Tsernogolu, Ph.D.	Physiology & Biophysics
Wilma White, B.A.	Pathology

Course in Compartmental Analysis, Spring 1970 (AMCS 525)

This is a new course which was developed to study critically some methods currently in use for the analysis of isotope tracer data from physiological and other intact systems. Topics: assumptions for tracer studies; differential equation formulation; fitting data with linear combinations of exponentials; integral equation formulation; relationship to network theory. The course was taught by Maxine L. Rockoff. Attending the course were:

James M. Baker, B.S.	BCL
Carol Coble, A.B.	BCL
Carol Cornwell, B.S.	Graduate Student
John Eichling, Ph.D.	Radiology
L. Holman, M.D.	Nuclear Medicine
Harold Law, M.S.	Graduate Student
Joanne Markham, B.A.	BCL
Douglas E. Mayfield, A.B.	Medical Student
Judy Metzger, M.A.	Radiology
Nizar Mullani, B.S.	BCL
Charles T. Patterson, M.S.	Graduate Student
Donald S. Quon, B.S.	Graduate Student

Course in Biomedical Mathematics, Fall, 1969

This is a new course which offers basic mathematics for investigators in the life sciences, with particular emphasis on the mathematics required in the formulation of kinetic models of physiological systems. Topics: logic, number systems, elementary algebra, trigonometry, complex numbers, vectors, matrices, calculus, and differential equations. The SCM Cogito 1016PR was used in laboratory sessions. The course was taught by Maxine L. Rockoff. Attending the course were:

Anita Birnberger, M.D.	Neurology
Karl L. Birnberger, M.D.	Neurophysiology
Robert Bricker, M.D.	Preventive Medicine

William Glenn, Jr., B.S.	BCL
John Halverson, M.D.	Surgery
Elizabeth Hilliker, A.B.	Medical Student
Leonard Jakubczak, Ph.D.	Physiology and Psychology, Veterans Administration Hospital, Jefferson Barracks, Missouri
Robert Laibovitz, A.B.	Medical Student
William B. Malarkey, M.D.	Metabolism
Bruce Ransom, B.A.	Neurosurgery
B. Ramanath Rao, Ph.D.	Ob/Gyn
Shabbir H. Safdar, M.D.	Medicine
Shirley Sahrmann, B.S.	Neurology
Paul Simpson, A.B.	Medical Student

VII. SEMINARS

During the year the following seminars were presented at BCL:

August 26, 1969 - "A Comparison of Exponential and Gaussian Analyses of Cerebral Clearance Curves," presented by Dr. Martin Reivich, Department of Neurology, Hospital of University of Pennsylvania, Philadelphia, Pennsylvania.

September 11, 1969 - "Electrocardiogram Rhythm Monitoring," presented by Mr. Ray Bonner, IBM Advance Systems Development, Yorktown Heights, New York.

October 22, 1969 - "Status Report on a Multilab Computer Center," presented by Dr. Josiah Macy, Jr., University of Alabama Medical Center, Birmingham, Alabama.

November 18, 1969 - "Interactive Computer Processing of Microscopic Images," presented by Mr. Kenneth S. Ledeen, Computer Systems for Medicine, Inc., Boston, Massachusetts.

January 15, 1970 - "Distribution of Blood Flow and Ventilation in the Lungs," presented by Dr. John B. West, Professor of Medicine & Bioengineering, School of Medicine, University of California, San Diego, California.

February 16, 1970 - "The Arpa Computer Network," presented by Dr. Robert Kahn, Consultant, Bolt, Beranek & Newman, Inc., Cambridge, Massachusetts.

March 26, 1970 - "Information Content of Data with Respect to Models," presented by Dr. Mones Berman, Mathematical Research Branch, National Institutes of Health, Bethesda, Maryland.

April 6, 1970 - "The Dynamics of Blood Flow in the Microcirculation," presented by Dr. Harold Wayland, Thomas Engineering Laboratories, California Institute of Technology, Pasadena, California.

May 13, 1970 - "Limitations on the Use of Gamma-Ray Cameras for Quantitative Studies," presented by Dr. Harold I. Glass, Hammersmith Hospital, London, England.

June 11, 1970 - "A Computer Controlled Electronically Deflectable X-Ray System," presented by Professor Osamu Fujimura, Research Institute of Logopedics and Phoniatrics, Faculty of Medicine, University of Tokyo, Japan.

VII. PAPERS AND PUBLICATIONS

The Biomedical Computer Laboratory has established a monograph series to systematize the many informal reports, reprints, program descriptions and other documents written at BCL or supported by some of the laboratory's facilities or staff. The list of monographs based on reports and articles prepared since the laboratory's inception in April, 1964, now stands at 139. Copies of the index to the BCL monograph series are available on request.

Publications and papers presented during the period covered by this report are listed below. In addition, a few papers now published, but not listed in previous reports are included.

Arnzen, R. J. and Swanson, W. M., "A Vascular System Simulator," presented at the Society of Engineering Science, Inc., 7th Annual Meeting, St. Louis, Missouri, November, 1969.

Arnzen, R. J. and Swanson, W. M., "Blood Flow Visualization in Large Vessels", presented at the Society of Engineering Science, Inc., 7th Annual Meeting, St. Louis, Missouri, November, 1969.

Barthel, G. R., "Computer Methods for Detection of Premature Ventricular Contractions in the Continuously Monitored Electrocardiogram," Washington University, St. Louis, Missouri, 1970 (M.Sc. Dissertation).

Cox, Jr., Jerome R., "Computer Monitoring of Electrocardiographic Rhythms," presented at the Society of Engineering Science, Inc., 7th Annual Meeting, St. Louis, Missouri, November, 1969.

Cox, Jr., Jerome R., Fozzard, Harry A., Nolle, Floyd M., and Oliver, G. Charles, "Some Data Transformations Useful in Electrocardiography," in Computers in Biomedical Research, Vol. 3, Stacy and Waxman, Editors, New York: Academic Press, Inc., 1969.

Cox, Jr., Jerome R., "Models and Data Acquisition in Auditory Physiology," in Biology and the Future of Man, Philip Handler, Editor, p. 551 ff, Oxford University Press, 1970.

Cox, Jr., Jerome R. and Hill, Rexford L., "Design Considerations for Interfacing Computers to Gamma-Ray Cameras," presented at the First Biennial Conference of Quantitative Organ Visualization in Nuclear Medicine, May 5-9, 1970, Miami, Florida. To be published.

Cox, Jr., Jerome R. and Medgyesi-Mitschang, Louis N., "An Algorithmic Approach to Signal Estimation Useful in Fetal Electrocardiography," IEEE Transactions on Bio-Medical Engineering, BME-16: 215, July, 1969.

Enoch, J. M., "Retinal Microspectrophotometer", Journal of Optical Society of America, 56: 833, 1966.

Finn, A. L., "The Kinetics of Sodium Transport in the Toad Bladder, II. Dual Effects of Vasopressin." Submitted for publication.

Finn, A. L. and Rockoff, M. L., "The Kinetics of Sodium Transport in the Toad Bladder, I. Determination of the Transport Pool." Submitted for publication.

Glenn, W. V., Bodicky, A. L., Feldman, A. and Glenn, R., "A Signal Plotter Operated Remotely Under the Control of a Small Computer. Presented at the Fifty-fifth Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, Illinois, November 30-December 5, 1969.

Holman, B. L., Agress, R. H., Hill, R. L., Potchen, E. J., "Relative Cerebral Blood Flow with an Intervenous Non-Diffusable Tracer; Theoretical Implications," submitted for publication to Investigated Radiology.

Holman, B. L., Hill, R. L., and Potchen, E. J., "Regional Cerebral Blood Flow with the Anger Camera, Part I, Software and Data Analysis," submitted for publication to Archives and Neurology.

Holman, B. L., Carter, C. C., Davis, D. O., Hill, R. L., and Potchen, E. J., "Regional Cerebral Blood Flow with an Anger Camera, Part II, Studies in Normal Man," submitted for publication to Archives and Neurology.

Holmes, W. F., "External Beam Treatment Planning with the Programmed Console," Radiology, 94: 391, February, 1970.

Holmes, W. F., "Low Resolution Mass Spectrometers," (Part of Chapter II, "Mass Spectrometer Data Acquisition and Processing Systems") in Biochemical Applications of Mass Spectroscopy, G. Waller, editor, in press.

Huang, S. C., Ghista, D. N., Cox, J. R. and Vayo, H. W., "A Method for Simultaneous Determination of 1) The Blood Flows to the Organs and 2) The Cardiac Output", submitted for publication.

Nabelek, I. and Nabelek, A., "Frequency Glides -- Their Spectra and Pitch Perception," Journal of the Acoustical Society of America, 47: 119, January, 1970. Presented at the 78th Meeting of the Acoustical Society of America in San Diego, California, November, 1969.

Nabelek, I., Nabelek, A., and Hirsh, I. J, "Pitch Perception of Two Types of Frequency Change: Glides and Jumps," Journal of the Acoustical Society of America, 47: 118, January, 1970. Presented at the 78th Meeting of the Acoustical Society of America in San Diego, California, November, 1969.

Nabelek I., Nabelek, A., and Hirsch, I. J., "Pitch of Tone Bursts of Changing Frequency," Journal of the Acoustical Society of America, 47: 8, 1970.

Potchen, E. J., Evens, R. G., Hill, R. L., Adatepe, M., Holman, L., Lindeman, J. and Markham, J., "Regional Pulmonary Function in Man; Quantitative Transmission Radiography as an Adjunct to Lung Scinti-scanning," The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 108: 724, 1970.

Powell, G. L., Elovson, J., and Vagelos, R. P., "ACYL Carrier Protein - XII. Synthesis and Turnover of the Prosthetic Group of ACYL Carrier Protein in Vivo," Journal of Biological Chemistry, 244: 5616, 1969.

Rockoff, M. L., "Fitting Data with Linear Combinations of Exponentials", presented at the Society for Industrial and Applied Mathematics 1970 National Meeting, June, 1970.

Snyder, D. L. and Goblick, T. J., "Analysis of Position Fix Accuracy Using High Altitude Satellites," M.I.T. Lincoln Laboratory, Technical Memoranda 41L-0200; May 1970.

Snyder D. L., Detection of Nonhomogeneous Poisson Processes Having Stochastic Intensity Functions," submitted to the IEEE Transactions on Information Theory for publication.

Snyder, D. L., "Estimation of Stochastic Intensity Functions of Conditional Poisson Processes," submitted to the IEEE Transactions on Information Theory for publication.

Snyder D. L., "Filtering for Independent Poisson Processes Having Stochastic Intensity Functions. To be presented at the UMR-Mervin J. Kelly Communications Conference, Rolla, Missouri, October 1970.

Snyder, D. L., "Parameter Estimation for Radioactive Tracer Data," to be presented at the UMR-Mervin J. Kelly Communications Conference, Rolla, Missouri, October, 1970.

Snyder, D. L., "Realization of Filter-Squarer Receivers," to appear in: IEEE Transactions on Information Theory, January, 1971. Presented at the 1970 International Information Theory Conference, The Netherlands, June, 1970.

Ter-Pogossian, M. M., Eichling, J. O., Davis, D. O., Welch, M. J., and Metzger, J. M., "The Determination of Regional Cerebral Blood Flow by Means of Water Labeling with Radioactive Oxygen-15," Radiology, 93: 31, 1969